# ANNALS OF THE RHEUMATIC DISEASES

# CHRONIC ABSORPTIVE ARTHRITIS OR OPERA-GLASS HAND:

## REPORT OF EIGHT CASES

BY

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Opera-glass hand, *la main en lorgnette*, has been described as a very rare condition. The term has been used only occasionally, but the disease to which it refers is neither so rare nor of such recent origin as is usually assumed. The present paper calls attention to reports of the same disorder under a variety of names, and describes eight additional cases from the authors' experience.

**Cases from the Literature.**—Marie and Léri (1913) described a 66-year-old woman with curious deformities of the hands. She had had severe generalized rheumatoid arthritis (*rhumatisme deformant generalisé*) for 28 years. Photographs of the hands showed that the fingers and wrists were shortened and contracted and the skin wrinkled, redundant, and thrown into transverse folds, giving the impression that the phalanges were retracted one into the other like an opera glass (*les phalanges étaient rentrées en lorgnette les unes dans les autres*). Dissection revealed that the phalanges had lost their normal shape, the regular cylinders had become irregular truncated cones, the articular ends had completely disappeared. These changes had been seen in a radiograph which showed similar absorption of bone at the distal ends of the radii, ulni, carpals, and metacarpals, and marked radiolucence of all the bones. Microscopic examination showed massive degeneration of bones, cartilage, and muscles sparing only the blood vessels, nerves, and tendons. The authors mentioned another patient with a similar deformity limited to one finger.

The term "doigts en lorgnette" was used by Brumpt (1906) to describe a deformity seen in a Sudanese Negro. The history was unreliable because of the ignorance and superstition of the patient and his associates. A line drawing of the hands showed most of the fingers to be markedly shortened, the skin soft and redundant, and the bones obviously shortened and distorted. The author stated that the fingers could be drawn out like a lorgnette and made to assume their normal length. The right ring finger and the left thumb and little fingers were normal. The hands were useless and the muscles were weak but not paralysed.

Weigeldt (1929) described a 64-year-old woman with "mains en lorgnette" whose arthritis began at 46. The photograph showed hands similar to those described by Marie and Léri. The published radiograph showed extensive bone destruction. A case published by Nelson (1938) showed similar areas of bone destruction and absorption. A parathyroid adenoma was discovered at autopsy,

FIG. 1.—Case 1. (B.O., male, 22.) Deformities of wrists, shortening of thumbs, distortion of all fingers with flexion deformities and lateral deviations of the proximal joints. Skin is loose, redundant, thrown into folds on the thumbs.

FIG. 2.—Case 1. Carpal bones practically disappeared. Distal ends of ulni come to a point. Ends of most of bones blunted or cupped out.

but whether this had any physiological significance might be questioned, since during the patient's last illness the serum calcium was 10·7 mg. per 100 ml., serum phosphorus 2·9 mg. per 100 ml., and phosphatase 3·6 units. Crain (1941) believed his case to be unusual because it was the first to be reported in a male. He was not aware of Brumph's patient.

The literature has also disclosed several cases showing extensive absorption of bone which have been variously called psoriatic arthritis, arthritis mutilans, and arthritis absorbans.

Adrian (1903) described a patient with psoriatic arthritis in which the radiographs showed extensive bone absorption involving the interphalangeal joints of all the fingers, and a similar but less extensive process in the distal interphalangeal joints. The metacarpal joints and the wrist joints were not seriously involved. The radiographs of the feet showed absorption of many bones of the toes. Shlionsky and Blake (1936) published radiographs of a case of psoriatic arthritis in which bone absorption was so extensive in the hands and feet as to suggest leprosy. Nielsen and Snorrason (1946) described four cases of arthritis mutilans with photographs and radiographs showing absorption such as has been described above. Fox and van Breemen (1934) reproduced radiographs of the hands showing absorption and fusion of the carpal bones, extensive absorption and subluxation, and grotesque deformities of the metacarpophalangeal joints. They described their case as one of "advanced rheumatoid arthritis in a young woman". Smyth (1949) described four cases of bone absorption and rheumatoid arthritis.

**Cases observed by the Authors.**—The authors have personally observed the following patients who are arranged according to the duration of their arthritis:

*Case 1. B.O.*, a 22-year-old white male, whose disease was characterized by a sudden onset, rapid extension to involve all joints within a few weeks, and continuous progression. He became bedridden within one year with marked deformity. Photographs of both hands (Fig. 1) three years after onset, show marked deformities, with enlargement of both wrists, shortening of both thumbs, and distortion of all fingers. The fingers show flexion deformities and lateral deviation. The skin is loose, redundant, and somewhat wrinkled. Radiographs of both hands (Fig. 2) show marked destruction and absorption of many bones. The distal end of both ulni are tapered. The carpal bones have practically disappeared. Most of the ends of the bones comprising the metacarpo-phalangeal joints have lost all semblance of their normal rounded shape, with the metacarpals flattened as though cut off, and the phalanges cupped out or excavated. There is definite overlapping in many instances. Similar changes are seen in the proximal interphalangeal joints.

*Case 2. E.C.*, a 29-year-old woman, whose arthritis began first in her hands. Her fingers were cold, clammy, and cyanotic, suggesting sclerodactylia and Raynaud's disease, for which bilateral dorsal sympathectomies were performed. She subsequently developed pulmonary tuberculosis. Photographs of both hands (Fig. 3, overleaf) five years after onset, in the right hand show flexion deformities and ulnar deviation, and in the left hand marked shortening of the thumb, and enlargement of the terminal phalanges strongly suggesting Heberden's nodes. Atrophy of the dorsal muscles of the hands and enlargement of the metacarpo-phalangeal joints may be noted. The skin is somewhat atrophic. Radiographs

FIG. 3.—Case 2. (E.C., female, 29.) Flexion deformities of many fingers. Ulnar deviation of fingers of right hand. Shortening of left thumb and enlargement of terminal joints suggesting Heberden's nodes.

FIG. 4.—Case 2. Incomplete destruction of all bones in thumbs. Absorption of the ends of many bones with cupping and subluxation.

of the hands (Fig. 4) show the distal ends of the forearms, wrists, and metacarpal bones to be approximately normal. The bones of both thumbs show destruction, with the left showing absorption of the distal half of the second phalanx and the proximal third of

the distal phalanx, and the right showing destruction of the joints. In the right hand the proximal phalanges show cupping and fusion of the proximal interphalangeal joints. There is also absorption of the bones comprising the distal joints of the fingers of the left hand with overriding.

*Case 3.* *O.K.*, a 45-year-old white female, with moderately severe arthritis of 10 years' duration, who is still ambulatory and does most of her housework. Fingers and toes show increased mobility of all the joints and are quite painful. The knees, wrists and elbows are swollen and tender, and have limited, painful motion. Photographs of both hands (Fig. 5) taken 10 years after onset, show shortening of the thumbs and fingers, with wrinkled and redundant skin. Radiographs (Fig. 6, overleaf) show absorption with tapering of the distal ends of both ulni, partial absorption and apparent fusion of the carpal bones, and absorption, cupping, and subluxation of the bones of the metacarpo-phalangeal joints of the right hand. A definite but not very extensive destructive process is also seen in the proximal interphalangeal joints of the fingers and the distal joint of the thumbs. In the left hand the metacarpo-phalangeal joints are only slightly involved, except for the left thumb which shows marked destruction and absorption of the distal half of the proximal phalanx and the proximal third of the distal phalanx. The proximal interphalangeal joints of the index, middle, and ring fingers show absorption. The distal joints of the fingers of the left hand show the characteristic absorption and cupping of the distal end of the middle phalanges, and some loss of the proximal end of the distal phalanges. Radiographs of both feet, not shown, have marked absorption, cupping,

FIG. 5.—Case 3. (O.K., female, 45.) Shortening of thumb and many fingers with wrinkling and redundancy of skin.

FIG. 6.—Case 3. Absorption and tapering of both ulni. Absorption and fusion of carpal bones. Absorption about metacarpo-phalangeal joints of right hand and proximal interphalangeal joints of left hand.

and overlapping of most of the metatarso-phalangeal joints, with complete disappearance of the distal half of the proximal phalanx of the left great toe, with absorption and cupping of the proximal end of the distal phalanx.

*Case 4. L.E.*, a white male, seen at age 36, whose arthritis began at age 22. He now has complete bony ankylosing of his ankles, knees, and hips, and marked flexion deformities of his elbows and hands. He has had iritis with subsequent loss of one eye. There are changes in his skin and particularly in the nails which are suggestive of psoriasis. Radiographs of both hands (Fig. 7) show absorption and tapering to a point of the lower ends of both ulni, and extensive absorption of the carpal bones, resulting in almost complete disappearance which is more marked on the right. The bones of both thumbs show extensive absorption and obvious shortening. The 3rd, 4th, and 5th fingers of the left hand, and the 4th and 5th fingers of the right hand demonstrate extensive absorption with cupping and subluxation. Most other joints of the fingers show rheumatoid arthritic changes. Both metacarpo-phalangeal joints of the index fingers are free of the absorptive process.

*Case 5. A.S.*, a white woman, 33 years old, whose arthritis began at 15 and who became bedridden at 18. The ankles, knees, hip, spine, wrists, and left elbow are firmly ankylosed. The shoulders and right elbow have marked limitation of motion. Both hands show distortion of wrists, shortening of thumbs, and flexion deformity of all except the left index finger. Abnormal range of motion of several fingers was present. Radiographs of both hands (Fig. 8) show severe demineralization of all bones. The left ulna

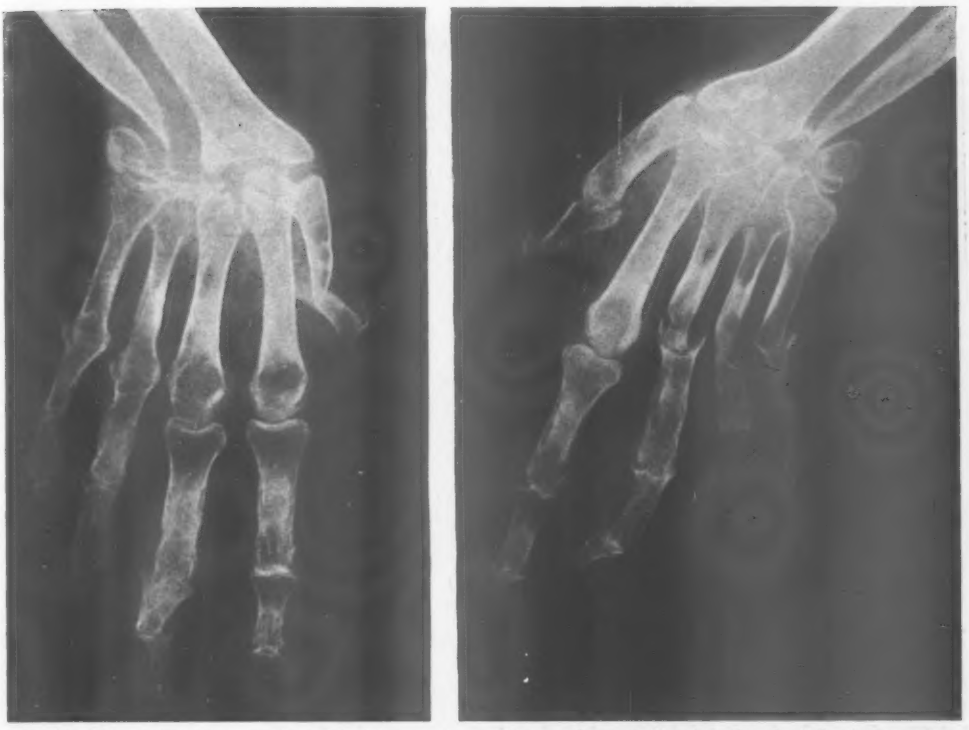

FIG. 7.—Case 4. (L.E., male, 36.) Absorption and tapering of distal ends of ulni. Absorption and fusion of carpal bones. Absorption of bones of both thumbs and about metacarpo-phalangeal joint of left third, fourth, and fifth fingers.

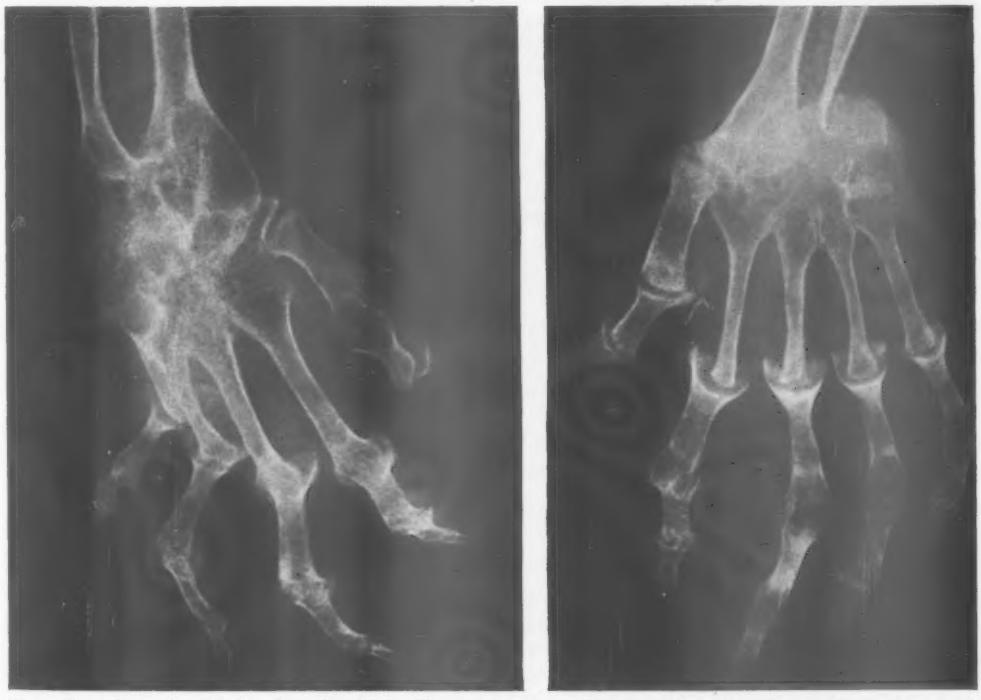

FIG. 8.—Case 5. (A.S., female, 39.) Severe demineralization of all bones. Absorption and fusion of wrists and bones about metacarpo-phalangeal joints of fingers.

FIG. 9.—Case 6. (C.S., male, 53.) Marked shortening and ulnar deviation of both wrists and shortening of all fingers. Skin is loose and thrown into folds. Nails show psoriatic-like lesions.

FIG. 10.—Case 6. Severe demineralization of all bones. Extensive absorption of wrists and all fingers of hands. Marked subluxation of metacarpo-phalangeal joints.

shows absorption with tapering to a point. The details of the bones in both wrists are completely obscured as though the carpal bones and the proximal ends of the metacarpal bones were fused into a solid bony mass. An absorptive process is apparent in all metacarpo-phalangeal joints. The normally rounded distal ends of the metacarpal bones have completely disappeared whereas the proximal phalanges show the marked cupping and

overlapping. The proximal interphalangeal joints of both hands show bony ankylosis with similar involvement of the distal joints.

*Case 6.* *C.S.*, a 53-year-old white male whose arthritis began at age 34. The disease progressed rapidly so that he was unable to walk within a few months of the onset. At present, with the exception of the joints of the hands, all the joints including the spine are ankylosed. He has lost the sight of both eyes due to cataracts. Photographs of both hands (Fig. 9) show marked ulnar deviation and shortening of the wrists with the skin of the fingers drawn up into folds. The fingers and thumbs are short because of changes in length of the phalanges. The nails and the adjoining skin show changes suggesting psoriasis. Radiographs of both hands (Fig. 10) show marked absorption of the distal ends of the bones in both forearms; the ulni taper to a point and appear to be approximately two inches shorter than the radii. The normal contours of the radii have been destroyed. The carpal bones have practically disappeared and those remaining are fused. Demineralization of the metacarpal bones and the phalanges is so marked that the details are obscured. The bones of the metacarpo-phalangeal joints have overlapped each other with the phalanges overriding about one third of the metacarpal bones. The middle phalanges have lost all semblance of normal contour, and appear almost egg-shaped in the right hand.

*Case 7.* *J.L.*, a 59-year-old woman, whose arthritis has been present for 26 years, having begun in the hands and spread to nearly all of the joints. Radiographs (Fig. 11) show generalized demineralization, destructive absorption of the lower ends of the bones of the forearms, marked loss of substance and fusion of the carpal bones, and marked absorptive changes in the metacarpal and phalangeal bones. The most marked absorption is in the bones of the proximal interphalangeal joints with the proximal phalanges, particularly on the left, showing loss of practically all of their bony substance and tapering

FIG. 11.—Case 7. (J.L., female, 59.) Severe demineralization of all bones. Absorption of bones, wrists and hands.

to a point. A destructive process is present in the other bones. Radiographs of the feet, not shown, have similar changes with marked subluxation of the proximal phalanges on the metacarpal bones.

*Case 8.* *C.D.*, a 67-year-old woman, whose arthritis began 42 years ago and who died shortly after admission to the hospital. Little is known about her clinical history. Photograph of both hands (Fig. 12) shows shortening of the wrists and fingers with marked redundancy of the skin. The fingers are markedly distorted with sharp angle deviations of many of the interphalangeal joints. The fingers showed abnormal range of passive motion in all directions and were useless to the patient. Radiograph (Fig. 13) shows severe demineralization of all bones, extensive absorption of the lower end of the left ulna, fusion and obvious loss of substance of the carpal bones, and extensive destruction and subluxation of all metacarpo-phalangeal and interphalangeal joints.

## Discussion

The eight cases described here include five women and three men. The age of onset ranges from 15 to 35 with an average of 24·6 years. The exact age at which the severe absorptive changes began or their exact duration are not known, but they were observed as early as 3 years after onset in Case 1, and have persisted as long as 42 years in Case 8.

The onset of the disease of these patients was typical of rheumatoid arthritis with a course which tended to conform to the more malignant type, so that six patients were bedridden and practically helpless in a relatively short time.

Two patients, Cases 4 and 6, showed changes of the fingernails and skin suggestive of psoriasis. The nails were rough, thick, irregular, friable, and separated from the nail bed. The skin about the fingernails was red, rough, and covered with yellow crusts. Lesions of the scalp, trunk, or extensor surfaces of the extremities, which one would expect in typical psoriasis were not present.

The condition of the finger and toe joints in this condition varies considerably from the usual findings of rheumatoid arthritis. In the typical rheumatoid arthritic the joints have limitation of motion or ankylosis, and the skin over the joints is usually contracted, thin, atrophic, pale, and shiny, and appears to be firmly attached to the bone. In contrast, most of the finger joints of the patients with this type of arthritis had an abnormal range of motion in all directions, and there was another striking feature in the ability of the fingers to elongate like a telescope when pulled out; the skin was loose, wrinkled, and thickened.

The absorption of bone is not that observed in rheumatoid arthritis, for although most rheumatoid arthritics do demonstrate absorption to a varying degree, in these cases, this process has advanced to extreme destruction with a loss in some instances of as much as half a bone. Yet another unusual feature is the fact that the process is confined to only one or two anatomical regions, with the other joints showing the characteristic changes of rheumatoid arthritis. Thus the loss of localized bone substance, the absence of fibrous contracture of the joint capsule and muscle tendons, and the flabbiness of the skin produce a picture which may be considered as either an unusual variant or as an extreme manifestation of rheumatoid arthritis.

FIG. 12.—Case 8. (C.D., female, 67.) Shortening of wrists and thumbs, and lateral deviation of proximal interphalangeal joints which are freely movable in all directions. Skin is loose, wrinkled, and redundant.

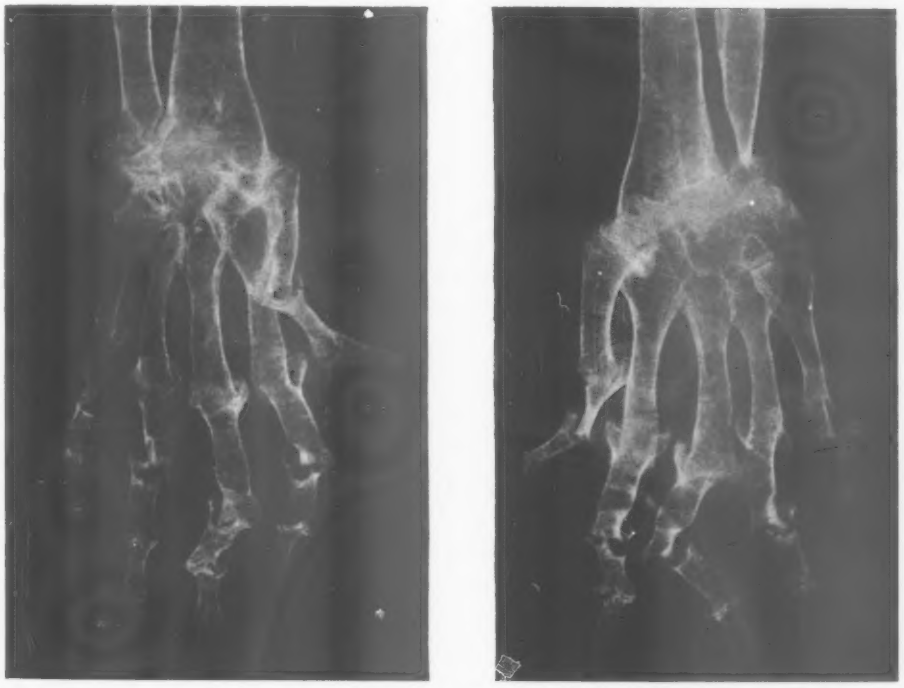

FIG. 13.—Case 8. Marked demineralization of all bones. Absorption and fusion of radii, ulni and carpal bones. Architecture of most of finger joints has been destroyed.

**Summary**

(1) Eight additional cases of chronic absorptive arthritis, the so-called *mains* or *doigts en lorgnette*, are described.

(2) The clinical features of these patients include generalized long standing severe rheumatoid arthritis with the additional extraordinary findings of shortening of fingers or wrists with increased range and direction of motion, redundancy of the skin, and extensive absorption of the bones of the affected joints.

(3) The condition may be considered as an unusual variant or as an extreme manifestation of rheumatoid arthritis.

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**Arthrite Absorbante Chronique ou "Mains en Lorgnette"**

RÉSUMÉ

(1) On relate huit cas additionnels d'arthrite absorbante chronique, nommée aussi "mains . . ." ou "doigts en lorgnette".

(2) Chez ces malades, souffrant depuis très longtemps d'une arthrite rhumatismale grave et généralisée, on a trouvé, en plus, des éléments cliniques extraordinaires: raccourcissement des doigts ou du poignet, augmentation de l'étendue et de la direction du mouvement, excès de peau et absorption considérable des os des articulations atteintes.

(3) On peut considérer cet état comme une variante peu commune ou bien une manifestation extrême de l'arthrite rhumatismale.

**Artritis Absorbente Cronica o Mano en Forma de Gemelos**

RESUMEN

(1) Se señala ocho casos adicionales de artritis absorbente crónica llamada también "mains . . ." o "doigts en lorgnette".

(2) En estos enfermos que sufrían desde mucho tiempo una arthritis reumatoide grave y generalizada se ha observado además ciertos elementos clínicos extraordinarios: acortamiento de los dedos y de la muñeca, aumentación de la extensión y de la dirección del movimiento, exceso de piel y absorción considerable de los huesos de las articulaciones afectadas.

(3) Se puede considerar esta condición como una variante poco común o una manifestación extremada de la artritis reumatoide.

# EXPERIMENTS IN GOLD-TESTING IN GOLD TREATMENT OF POLYARTHRITIS

BY

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Gold salts are still the best of all the therapeutic agents used in the treatment of chronic polyarthritis. Complications of varying degrees of severity are encountered in about 50 per cent. of the cases so treated. A mild complication, however, usually causes the patient only slight discomfort, particularly as most often his rheumatic distress simultaneously undergoes rapid alleviation for a shorter or longer period.

Nevertheless, in certain cases a serious, occasionally very painful, diseased condition develops which proves far worse than the distress for which the patient in question sought medical aid. As a result gold-treatment has not won the popularity it deserves, a circumstance which the good results obtained with BAL do not yet seem to have altered. A negative attitude to gold therapy is also natural in those cases in which complications arise some time after the patient's discharge. Many such cases ignore their symptoms as long as possible, not understanding their seriousness, with the result that a long period elapses before their distress can be alleviated by expert care. Inasmuch as there is no way of foreseeing such a development after gold therapy, an element of uncertainty is involved, disagreeable to both physician and patient.

There is much to indicate that these cases arise from a straightforward allergy to the gold salt used. Thus it should be possible to ascertain by a test which patients are hypersensitive to gold and thus likely to suffer such complications.

In the relatively scanty literature on these problems, dermatitis has attracted particular attention. Lichtenstein and Stillians (1935) used a patch test with 33 per cent. gold sodium thiosulphate in wool fat. They obtained positive reactions in over one hundred cases, all of which had a rash during gold treatment. In addition, they obtained positive reactions in 40 per cent. of the total number of cases treated with gold sodium thiosulphate, in 25 per cent. of which dermatitis developed. They do not, however, state whether the tests were performed before, during, or after the gold therapy, or whether a positive reaction indicated a complication which set in later.

Schwatt and Rest (1937) used an ointment consisting of one part sanocrysin to two parts lanolin with negative results.

Some investigators have attempted intracutaneous testing with gold salts (Lebeuf (1932) and Gaté, Cuilleret, and Tiran (1932), among others), but these report limited experimental series, with only a few tests in each case, and with negative results.

## Methods

For the past eighteen months we of the Pensions Board Department at the Norrköping Hospital have regularly carried out intracutaneous tests with gold sodium thiosulphate on all newly-admitted patients. In the course of our experiments we have used 1 : 1, 1 : 3, 1 : 5, and 1 : 10 dilutions of aurothion (Astra); for purposes of control we used the same dilutions of 6·5 per cent. sodium thiosulphate solution. The strength of this control solution was based on the amount of free sodium thiosulphate in aurothion.*

Between 0·02 and 0·05 ml. of each dilution was injected intracutaneously, usually on the back, so that the papules were 5 mm. in diameter. Readings were taken after 20 to 30 minutes. An oedematous papule of from 5×5 to 10×10 mm., with a more or less reddened marginal zone, was recorded as (+), a papule of from 10×10 to 15×15 as +, and a papule of from 15×15 to 20×20 as ++, in accordance with the marking system ordinarily used in the diagnosis of allergies.

## Results

In the beginning we expected that when the aurothion solution was diluted to a certain point we should obtain a positive reaction indicating the probability of later complications in connection with the gold therapy. We were unable, however, to establish any definite relationship in this respect. Complications were as likely to occur in cases with weakly positive reactions at the beginning of the course of treatment as in cases with strong reactions. Six months ago we began to give our patients further tests during treatment. It then appeared that their reactions often changed from positive to negative or from negative to positive, and that in the latter case some complication often set in while the patient was in hospital.

Our series is as yet limited, but I felt it desirable to report on these preliminary results, because I know that several colleagues have expressed the need of a method of this type by which the danger of complications might perhaps be reduced.

From the beginning of our re-testing during therapy from March to the middle of September, 1949, we have had 69 in-patients, each receiving gold therapy during

TABLE I

PATIENTS INCLUDED IN TEST SERIES

| Time of Gold Therapy | Patients Free of Symptoms | Complications | | Total |
|---|---|---|---|---|
| | | During Therapy | After Therapy | |
| March to September .. | 29 | 10 | 11 | 50 |
| October .. .. .. | — | 6 | — | 6 |

* The firm of A. B. Astra was kind enough to provide us with these solutions when it proved difficult to make them sterile without precipitating the sodium in the solution.

a 2-months' stay in hospital. All were recently sent questionnaires on their condition after discharge and on the medical care received, if any. Thereafter a diagnosis and description of each case was obtained from the physician in charge. A number of persons were examined. In only one case was no information obtained.

Of the remaining 68, it was found that 25 (37 per cent.) had incurred some complication during or after gold therapy. Fifty had been tested twice or more during their stay in hospital; the whole investigation includes this group of fifty, and six other cases treated more recently, in whom complications set in during gold therapy (Table I). For those who underwent follow-up examinations, the observation period was six weeks to two months in five cases and over two months in 45 cases.

As Table I shows, about half of the complications developed after discharge. Two of these had severe dermatitis, one being hospitalized for two weeks and the other being treated for six weeks in the Out-patient Department.

Tables II and III show the nature of the reactions from the first to the second test in those cases which showed the least or greatest change in the amount of

TABLE II

GREATEST AND LEAST CHANGES IN REACTION IN CASES WITHOUT COMPLICATIONS

| Reaction | Record No. | Test No. 1 | | | | Test No. 2 | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 1 : 1 | 1 : 3 | 1 : 5 | 1 : 10 | 1 : 1 | 1 : 3 | 1 : 5 | 1 : 10 |
| Decreased .. | 105 | (+) | — | — | — | — | — | — | — |
| | 74 | + | + | (+) | (+) | (+) | — | — | — |
| Unchanged .. | 189 | (+) | — | — | — | (+) | — | — | — |
| | 178 | + | + | (+) | — | + | + | (+) | — |
| Increased (1 case) .. | 127 | (+) | (+) | — | — | + | (+) | (+) | — |

TABLE III

GREATEST AND LEAST CHANGES IN REACTION IN CASES WITH COMPLICATIONS

| Reaction | Record No. | Test No. 1 | | | | Test No. 2 | | | | Complication |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 : 1 | 1 : 3 | 1 : 5 | 1 : 10 | 1 : 1 | 1 : 3 | 1 : 5 | 1 : 10 | |
| Decreased (1 case) .. | 215 | + | — | — | — | (+) | — | — | — | Transitory leucopenia |
| Unchanged .. | 136 | (+) | — | — | — | (+) | — | — | — | Dermatitis |
| | 114 | + | (+) | (+) | — | + | (+) | (+) | — | |
| Increased .. | 113 | (+) | — | — | — | (+) | (+) | — | — | |
| | 50 | + | + | — | — | + | + | + | (+) | |

reaction, in cases without complications and in cases with complications. The results have been subdivided into three categories: decreased, unchanged, and increased reaction.

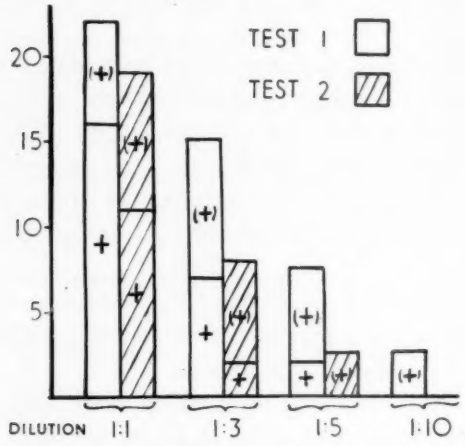


FIG. 1.—Number of positive and weakly positive reactions with varying dilutions of aurothion in cases *without* complications.

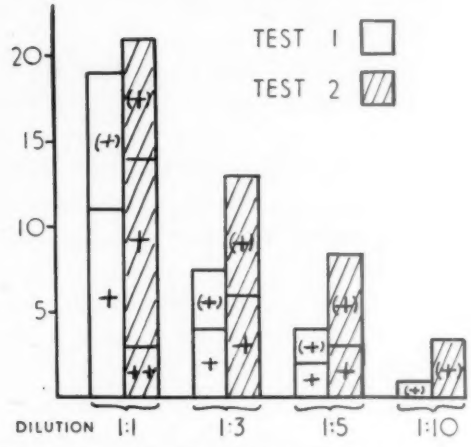


FIG. 2.—Number of positive and weakly positive reactions with varying dilutions of aurothion in cases *with* complications.

Figures 1 and 2 show the total number of weakly positive and positive reactions in the first and second tests, both in cases without and cases with complications. A + reaction was given a value of 1, a (+) reaction a value of 0·5, and a ++ reaction a value of 1·5, according to their size relationships. The graph shows that in those cases in which gold therapy was not followed by complications and reactions decreased or disappeared—in other words, during treatment a certain desensitization took place. In those cases in whom complications ensued, on the other hand, the reactions increased or became positive in the weaker dilutions.

TABLE IV

COMPARISON BETWEEN CHANGE IN REACTION IN CASES WITHOUT AND CASES WITH COMPLICATIONS

| Change in Reaction | Without Complications | | With Complications | | Total No. of Cases |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| Decreased .. .. | 19 | 95 | 1 | 5 | 20 |
| Unchanged .. .. | 9 | 57 | 7 | 44 | 16 |
| Increased .. .. | 1 | 5 | 19 | 95 | 20 |
| Total .. .. | 29 | — | 27 | — | 56 |

Our results appear most clearly in Table IV, in which the numbers of cases with reduced, unchanged, and increased reactions are tabulated and subdivided into the two main groups with and without complications. Complications followed

in only 5 per cent. of cases with decreased reaction, in 44 per cent. of cases with unchanged reaction, and in 95 per cent. of cases with increased reaction. Thus in the first and last of these three groups, which together total forty out of 56 (71 per cent.) the change in reaction seems to have given an accurate indication.


## Summary

A gold-testing method is described, by means of which one should be able to form an accurate idea of the danger of complications in about two-thirds of all gold treatments. Out of 56 cases tested an increased reaction was followed by complications in nineteen out of twenty cases, and a decreased reaction was followed by no complications in nineteen out of a further twenty cases. Of the remaining sixteen cases which showed no change in reaction, seven (44 per cent.) had complications, and nine (57 per cent.) had none.


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### Expériences avec le Test Aurique dans la Chrysothérapie de la Polyarthrite


Résumé

On décrit un test aurique au moyen duquel on peut se faire une idée exacte du danger de complications dans les deux tiers des cas de chrysothérapie. Ce test fut appliqué chez 56 malades. La réaction augmentée chez 20 malades fut suivie de complications chez 19 d'eux; la réaction diminuée chez 20 autres malades ne fut suivie d'aucune complication chez 19 d'eux. Sur 16 cas dans lesquels la réaction n'avait pas varié, sept d'eux (44%) eurent des complications, et les neuf autres (56%) n'en eurent pas.


### Experimentos con la Prueba Aurica en la Crisoterapia de la Poliartritis


Resumen

Se describe una prueba áurica que permite señalar en las dos terceras de los casos el peligro de complicaciones en el curso de crisoterapia. Esta prueba fué aplicada en 56 casos. La reacción aumentada en 20 casos fué seguida de complicaciones en 19 de ellos; una reacción disminuida en otros 20 casos no fué seguida de complicación alguna en 19 de ellos. En 16 casos la reacción permaneció sin cambiar; hubo complicaciones en siete (44%) de ellos y no las hubo en los demás 9 (56%).

# A STUDY OF THE INTERRELATIONS OF RHEUMATOID ARTHRITIS AND DIABETES MELLITUS

BY

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In investigations on the interrelations of rheumatoid arthritis and the various endocrine disturbances, very little attention has been paid to diabetes mellitus. Thus, there exist only short notes on the occurrence of rheumatoid arthritis among diabetics (Wolf, 1936), and only the effects of an insulin treatment given to rheumatoid arthritis patients have been subjected to a closer examination (Copeman, 1946). A further reason for analysing the interrelations of rheumatoid arthritis and diabetes mellitus was that an increased secretion of the *adrenocortical glucocorticoids* (as cortisone or Compound E) and of the *antehypophyseal hormones* (ACTH) is at present regarded as a feature of diabetes mellitus; and these hormones are those upon which the interest in rheumatoid arthritis is now concentrating.

## Material

The study comprises the rheumatoid arthritis and diabetes mellitus patients treated at the Third Medical Clinic of the University of Helsinki and in the medical wards of the Kivelä Hospital during the 15-year period 1934-1948.

**Rheumatoid Arthritis Patients.**—There were 1,008 in this group, of whom 725 were female and 283 male. The average age in the whole group was 48·7 years.

**Diabetes Mellitus Patients.**—There were 766 altogether, of whom 490 were female and 276 male. The average age was 51·6 years.

## Rheumatoid Arthritis and Diabetes Mellitus occurring in the same Patient

In the present series, $1 \cdot 3 \pm 0 \cdot 36$ per cent. of the rheumatoid arthritis patients were affected with diabetes mellitus, and $1 \cdot 7 \pm 0 \cdot 47$ per cent. of the diabetes mellitus group suffered from rheumatoid arthritis.

In order to know whether the present results show that these two diseases have a tendency either to occur together more often than is due to pure chance, or to avoid each other, the figures should be compared with the corresponding morbidity rates among similar population groups.

According to earlier studies (Järvinen, 1950) the frequency of rheumatoid arthritis in Helsinki is $0 \cdot 94 \pm 0 \cdot 35$ per cent. in control material, corresponding in sex distribution with the diabetes group in question. However, the average age in this control group was only 36 years. In view of the studies of the age distribution

of rheumatoid arthritis (Edström, 1939), the frequency of rheumatoid arthritis will be expected at approximately 1·8 per cent. in the diabetes group in question (average age 51·6 years). This figure corresponds with earlier studies in Finland (Holsti and Rantasalo, 1936).

Among the control material there occurred 0·54±0·27 per cent. of diabetes mellitus. This control group consisted of the cases of typhoid, paratyphoid, and acute gastro-enteritis which were treated in Kivelä hospital from 1934 to 1948. They totalled 748 persons of whom 522 were female and 226 male, the average age being 35·9 years. According to the age- and sex-distribution tables of Joslin and others (1947) this result corresponds with a diabetes frequency of 1·4 per cent. in a group of an average age of 48·7 years, in which approximately three-quarters are women. This figure approximates to those given in studies on the frequency of diabetes mellitus in various countries (Joslin and others, 1947).

**Result.**—As is shown above, 1·3±0·36 per cent. of the patients of the present series suffering from rheumatoid arthritis were also affected with diabetes mellitus, whereas the occurrence of diabetes mellitus in a corresponding group was assessed at 1·4 per cent. 1·7±0·47 per cent. of the diabetes mellitus patients of the series suffered from rheumatoid arthritis, whereas the estimated occurrence of rheumatoid arthritis in a corresponding group of people was approximately 1·8 per cent.

Considering the many sources of error (it must be noted, for instance, that the study was concerned only with hospital patients), the present results show at least that these two diseases have no obvious tendency either to occur together, or to avoid each other.

## Mutual Effects of Rheumatoid Arthritis and Diabetes Mellitus occurring in the same Patient

Rheumatoid arthritis and diabetes mellitus occurred in the same patient in thirteen of the present cases. An attempt has been made to elucidate the inter-relations of these two diseases with the aid of the Table overleaf.

Among the patients affected with both rheumatoid arthritis and diabetes mellitus, were some in which the rheumatoid arthritis began first and some in which the diabetes mellitus began first. *In most cases, the disease first acquired appeared to proceed as before, unaffected by the new illness.* In two cases, there was a distinct exacerbation of the symptoms of rheumatoid arthritis at the onset of diabetes mellitus. Conversely, in one case, diabetes mellitus was aggravated by the onset of rheumatoid arthritis. It must also be noted that, in one case, both diseases seemed to appear at the same time.

## Discussion

At the present time, it is usually thought that in many cases of diabetes mellitus, the secretion of the antehypophyseal hormones, in particular that of ACTH, and of the adrenocortical glucocorticoids is increased. This is regarded as being especially

true of the type of diabetes which begins in middle age, and is associated with obesity and arterial hypertension. In addition to the numerous investigations supporting this view which have been presented in the textbooks, it may be mentioned that, analogously with the earlier animal experiments, it has recently been noted that ACTH as well as cortisone is able to produce symptoms of diabetes mellitus in man (Boland and Headley, 1949; Brøchner-Mortensen and others, 1949; Conn and others, 1948).

TABLE

PATIENTS AFFECTED WITH BOTH RHEUMATOID ARTHRITIS AND DIABETES MELLITUS

| Groups of Patients | | Rheumatoid Arthritis began first (7) | | | | | | | Diabetes Mellitus began first (5) | | | | | Both diseases began simultaneously (1) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sex | | M. | M. | F. | F. | F. | F. | F. | F. | F. | F. | F. | M. | F. |
| Age | at onset of R.A. | 34 | 35 | 36 | 43 | 44 | 51 | 53 | 53 | 53 | 58 | 60 | 61 | 60 |
| | at onset of D.M. | 62 | 63 | 38 | 72 | 48 | 54 | 65 | 49 | 40 | 48 | 44 | 56 | 60 |
| Use of insulin | | No | at times | at times | No | continuously | No | at times | at times | continuously | No | No | at times | at times |
| Height (cm.) | | 173 | 182 | 153 | 154 | Thin | 170 | Fat | 162 | 165 | 157 | 162 | 170 | 158 |
| Weight (kg.) | | 90·5 | 75 | 66·3 | 67·5 | | 69 | | 66 | 61·5 | 54·9 | 105 | 74·9 | 61 |
| Blood pressure (mm. Hg) | | 160/110 | 180/100 | 220/110 | 150/80 | 120/80 | 160/110 | 160/110 | 240/120 | 160/100 | 250/120 | 205/110 | 190/90 | 130/70 |
| R.A. with obvious active swellings in joints during D.M. | | No | Yes | No | No ? | Yes ? | Yes | Yes ? | Yes | Yes | Yes | Yes ? | Yes | Yes |
| Changes in first disease at onset of the second disease | | 0 | + | 0 | 0 | 0 | + | 0 | + | 0 | 0 | 0 | 0 | + |

0=no changes.
+=activation of symptoms.

Therefore it may be assumed that the secretion of the antehypophyseal hormones (ACTH) and of the adrenocortical glucocorticoids (cortisone) has been pathophysiologically increased in at least some of the thirteen diabetes-rheuma patients (most of whom suffered from the type of diabetes commencing in middle age), and is associated with obesity and arterial hypertension (this was seen in seven distinctly, and four somewhat less clearly).

On the other hand, the present investigations show that the onset of diabetes mellitus did not effect a recovery from a simultaneous rheumatoid arthritis, and did not even prevent the onset of rheumatoid arthritis. This finding suggests that even a pathophysiologically increased secretion of ACTH and of glucocorticoids (cortisone) has no curative effect on rheumatoid arthritis.

Thus it seems strange that a rapid recovery from the symptoms of rheumatoid arthritis can be effected by administering *massive* doses of ACTH or cortisone, as has been shown by the revolutionary experiments of Hench and others (1949).

It is, therefore, advisable to think that the *manifest effects of massive doses of these hormones depend on something other than their simple physiological hormonal actions.* This is suggested also by the experience of Hench and others (1949) that smaller doses of these hormones have no curative effect.

In studying the difference between the physiological action of these hormones and the effect of massive doses of them, it is worth noting that, *in connexion with a massive administration of ACTH or cortisone to rheumatic patients, the development of symptoms suggesting an atrophy of the adrenal cortex has been observed,* corresponding to the results of animal experiments (Sprague and others, 1950). From this observation a parallel may be drawn between the advantageous effects of massive doses of cortisone and the theories of Selye (1946). The increased secretion of the mineralocorticoid, desoxycorticosterone, which Selye regards as an essential factor in the aetiology of rheumatism, would be reduced by the atrophy of the adrenal cortex caused by massive doses of cortisone and thus a favourable effect would be obtained.

**Summary**

(1) The interrelations of rheumatoid arthritis and diabetes mellitus have been studied in 1,008 cases of rheumatoid arthritis, and 766 cases of diabetes mellitus. An analysis of this material suggests that the occurrence of these two diseases in the same person corresponds with the average occurrence of both the diseases in the population in general. Accordingly, these diseases seem to have no tendency either to occur together or to avoid each other.

(2) Thirteen cases, in which the same patient was affected with both rheumatoid arthritis and diabetes mellitus, were subjected to a more detailed analysis: in nine there was no evidence of a mutual effect of the diseases upon each other; in two cases of rheumatoid arthritis, the symptoms were aggravated simultaneously with the onset of diabetes mellitus; in one case of diabetes mellitus the symptoms were exacerbated at the onset of rheumatoid arthritis. In one case, both diseases began at the same time.

(3) The present findings (which show that diabetes mellitus seems to have at least no curative action on rheumatoid arthritis) are compared with the modern view, according to which diabetes mellitus is closely associated with an increased secretion of the anterior hypophyseal adrenocorticotrophic hormone (ACTH), and of the adrenocortical glucocorticoids (as cortisone). Since, however, massive doses of ACTH and cortisone are known to give rapid relief to the symptoms of rheumatoid arthritis, the writer's interpretation is that these hormones have a different action according to whether they are administered in physiological or in massive doses. An attempt is made to explain this difference by the suggestion that the massive dosage of these hormones acts on rheumatoid arthritis through those disturbances which it is known to cause in the hormonal secretions of the organism.

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## Étude du Rapport entre l'Arthrite Rhumatismale et le Diabète Sucré

RÉSUMÉ

(1) Cette étude porte sur 1,008 cas d'arthrite rhumatismale, et sur 766 cas de diabète sucré. L'analyse de ce matériel suggère que l'incidence de ces deux maladies chez les mêmes sujets correspond au multiple de leur incidence respective générale, c'est à dire qu'elles n'ont pas tendance à se présenter ensemble ni à s'éviter.

(2) L'analyse détaillée de treize cas d'arthrite rhumatismale et de diabète sucré coëxistant chez le même sujet ne révéla aucun indice d'influence d'une maladie sur l'évolution de l'autre dans neuf cas; dans deux cas d'arthrite rhumatismale il y eut une aggravation des symptômes coincidant avec le début du diabète; dans un cas de diabète sucré les symptômes s'aggravèrent au début de l'arthrite rhumatismale; dans un cas les deux maladies débutèrent en même temps.

(3) On discute ces résultats (montrant que le diabète sucré ne semble exercer aucune action curative sur l'arthrite rhumatismale) à la lumière des conceptions modernes, selon lesquelles le diabète serait étroitement associé à l'augmentation de la sécrétion de l'hormone adrénocorticotrophique pituitaire antérieure (ACTH) et des glucocorticoïdes surrénaux, comme le cortisone. Sachant, cependant, que des doses massives de l'ACTH et du cortisone font disparaître rapidement les symptômes de l'arthrite rhumatismale, les auteurs pensent que l'action de ces hormones en doses physiologiques diffère de leur action en doses massives. Pour expliquer cette différence on suggère que les doses massives de ces hormones agissent sur l'arthrite rhumatismale par le fait qu'ils provoquent le dérangement bien connu des sécrétions hormonales de l'organisme.

## Estudio de la Relacion entre la Artritis Reumatoide y la Diabetes

RESUMEN

(1) Este estudio comprende 1,008 casos de artritis reumatoide, y 766 casos de diabetes. El análisis de este material parece mostrar que la incidencia de ambas enfermedades en un sujeto corresponde a su incidencia general y que, por consiguiente, estas enfermedades no tienen tendencia à presentarse juntas ni a evitarse.

(2) Se ha estudiado con interés particular trece casos de coexistencia de la artritis reumatoide y de la diabetes en el mismo sujeto. En nueve casos no se encontró indicios de influencia de una de estas enfermedades sobre la evolución de la otra. En dos casos de artritis reumatoide hubo agravación de síntomas coincidente con el principio de la diabetes. En un caso los síntomas de la diabetes empeoraron al principiar la artritis reumatoide. En un caso ambas enfermedades empezaron al mismo tiempo.

(3) Se discute estos resultados (mostrando que la diabetes no parece ejercer acción curativa alguna sobre la artritis reumatoide) en relación con las concepciones modernas según las cuales la diabetes estaría estrechamente liada al incremento de la secreción de la hormona adrenocorticotrófica hipofisaria anterior (ACTH) y de los glucocorticoides sobrerrenales, como el cortisón. Sabiendo, sin embargo, que dosis fuertes de ACTH y del cortisón alivian rapidamente los síntomas de la artritis reumatoide, se considera que estas hormonas ejercen una acción diferente según se las administra en dosis fisiológicas o en dosis fuertes. Para explicar esta variación de efectos se sugiere que dosis fuertes de estas hormonas actuan sobre la artritis reumatoide como consecuencia del conocido disturbio de las secreciones hormonales del organismo.

# ANKYLOSING SPONDYLITIS IN SISTERS

BY

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The incidence of ankylosing spondylitis appears to be on the increase and during the recent war a large number of cases was observed among the forces. Boland and Present (1945) reported that 18 per cent. of soldiers admitted to a U.S. Army General Hospital with chronic back complaints were found to have this disease. Graham and Ogryzlo (1947) also noted in the Toronto Arthritis Centre the high ratio of one case of ankylosing spondylitis to every 2·8 cases of rheumatoid arthritis. This apparent increase in the incidence of the disease is undoubtedly due, in part, to quicker diagnosis, with the result that many cases which have not advanced beyond a very early stage are now being recognized.

Ankylosing spondylitis is predominantly a disease of young men. Buckley (1931) reported a sex incidence of ten males to one female. This is the average figure given, although Graham and Ogryzlo (1947) reported a ratio of 16 to 1 and Bauer (1939) 20 to 1 respectively in their series. On the other hand, Fletcher (1944) found that 47 per cent. of 68 patients with the disease were females, a finding which he was unable to explain. The sex incidence in my own series was three males to one female.

Evidence is available, though by no means conclusive, to support the view that ankylosing spondylitis is a familial disease (Stecher and Hauser, 1946; Campbell, 1947; Rogoff and Freyberg, 1949) and its occurrence in brothers has been reported from time to time. Ray (1932) recorded the disease in twin brothers; Stecher and Hauser (1946) also described two brothers and cited three other instances of the disease affecting brothers. Campbell (1947) stated that in his series of 25 cases two of his patients were identical male twins, another two were brothers, a fifth had a brother who had died from the disease, and a sixth had an uncle and a brother with the disease. Tegner and Lloyd (1949) noted that all three children of one family (two brothers and a sister) were suffering from ankylosing spondylitis.

The occurrence of ankylosing spondylitis in sisters, however, is so rare that the presentation of the following is thought to be justified. I have noticed only one report in the literature of the disease affecting sisters (Scott, 1942), but no details are given. This rarity of " sister " cases might, of course, reasonably be explained by the low incidence of the disease in females.

## Case Histories

The family history is as follows. The patients' father, mother, two brothers, and two sisters are alive and well. The mother had rheumatic fever at the age of 28, and one brother and one sister show evidence of old healed rickets. The members of the family as a whole are of short stature.

**Case 1.**—Single, aged 31, clerk. Previous health: chickenpox, measles, whooping-cough, and rickets, as a child.

*History.*—The first symptom of ankylosing spondylitis appeared in 1936, when at the age of eighteen she noticed that her lumbar spine was stiff but not painful. The stiffness disappeared without treatment after six weeks, but returned a year later and has been present since. About this time her doctor accidentally discovered that she had an endocarditis. Shortly afterwards she developed a dull ache in the lumbar region. From then on the disease slowly progressed to involve the sacro-iliac joints, the dorsal and cervical vertebrae, the shoulders, hips, and temporo-mandibular joints. No history of iritis. During the course of the disease she received various forms of treatment, including bed-rest, deep *x*-ray therapy, physiotherapy, and spinal supports. At present she complains of a slight ache in the lumbar spine, and stiffness in the spine as a whole, and in the shoulders, hips, and jaws.

*Present Condition.*—Height 4 ft. 7 in., weight 6 st. 2 lb., E.S.R. (Westergren) 44 mm. Standing erect the patient shows dorsal kyphosis, forward inclination of the cervical spine, slight hyper-extension of the head, flattening of the lumbar spine, shortening of the femora, and anterior bowing of both tibiae. The head is slightly tilted to the right and movement of it is impossible, the cervical spine being immobile. The lower jaw has receded because of involvement of the temporo-mandibular joints and its range of movement is limited to 1 in. There is slight limitation of movement at the shoulder and elbow joints. All movements of the hip joints are considerably restricted, especially abduction which is limited to 30°. There is tenderness on pressure over the ischial tuberosities. Chest expansion is 1 in. All the other joints, including those of the hands, appear to be unaffected. Systolic and presystolic murmurs at the mitral area are heard and confirmed by phonocardiogram. Blood chemistry—serum calcium 10 mg. per 100 ml.; inorganic phosphate 4·5 mg. per 100 ml.; alkaline phosphatase 8 units (Kay).

*Radiological Findings.*—The appearances are those of advanced ankylosing spondylitis involving the whole of the spine (Fig. 1) with extreme osteoporosis of the vertebral bodies, complete obliteration of the sacro-iliac joints and the apophyseal joints, and calcification in the anterior common ligament and in the ligaments and capsules of the facet joints. Erosion of bone is seen in the pubic rami, ischial tuberosities, the greater and lesser trochanters and the 6th and 7th cervical spinous processes. Narrowing of joint space is seen in the shoulder, hip, and temporo-mandibular joints. There is evidence of old rickets of the femora, tibiae and fibulae.

**Case 2.**—Single, aged 29, clerk. Previous health: measles as a child.

*History.*—The earliest symptom of ankylosing spondylitis appeared in 1939, when at the age of 19 she developed pain down the back of both legs. This cleared up completely after bed-rest for six weeks. About a year later she noticed a stiffness in her neck, shoulders, and lower back, and this was accompanied by girdle pains. The disease slowly spread and in 1943 her neck became very painful. In 1945 the finger joints began to be painful and swollen and she experienced considerable pain in both hips, especially the right, and the temporo-mandibular joints. No history of iritis. During the course of the illness she received bed-rest, several courses of deep *x*-ray therapy and physiotherapy, injections of myocrisin, and spinal supports. At present she complains of pain

FIG. 1.—Case 1, showing advanced degree of ankylosing spondylitis. Note (*a*) sclerosis in iliac bones, and (*b*) erosions of bone at ischial tuberosities, and greater and lesser trochanters.

in both hip joints, particularly in the right, and stiffness of the neck, lower back, and fingers.

*Present Condition.*—Height 4 ft. 11 in., weight 7 st. 3 lb., E.S.R. (Westergren) 18 mm. Standing erect the patient shows moderate kyphosis of the dorsal spine, forward inclination of the cervical spine, and slight hyperextension of the head. The normal lumbar lordosis is still present. All head movements are considerably restricted. There is some pain in the temporo-mandibular joints on opening the mouth to its full extent, but the jaw movements are full. A little swelling of the proximal interphalangeal joints of the index and middle fingers of both hands and a moderate degree of interosseal wasting is present. There is tenderness on pressure over the ischial tuberosities and the greater trochanter on both sides. The hip movements are full, but accompanied by some pain on abduction. Chest expansion is limited to $\frac{1}{2}$ in. All the other joints appear to be intact. A basal systolic murmur is present. Blood chemistry—serum calcium 10·4 mg. per 100 ml.; inorganic phosphate 3·9 mg. per 100 ml.; alkaline phosphatase 5 units (Kay).

*Radiological Findings.*—The appearances are those of a moderately advanced ankylosing spondylitis. There is complete obliteration of both sacro-iliac joints and involvement of the apophyseal joints of the lumbar, dorsal, and cervical vertebrae (Fig. 2, overleaf). Calcification of the anterior common ligament in the cervical spine and of the lateral ligaments in the lower lumbar region is present. Irregularity of the symphysis pubis, the ischial tuberosities, and both greater trochanters is seen. *X* ray of the hands shows some soft-tissue swelling of the fingers, and decalcification of the phalanges and metacarpal

FIG. 2.—Case 2, showing involvement of cervical spine.

FIG. 3.—Case 2, showing (*a*) erosion of greater trochanter, and (*b*) calcification in gluteus minimus.

bones, but no loss of joint space. There are no radiological changes in the temporo-mandibular, shoulder, or hip joints. Calcification in the attachment of the gluteus minimus to the greater trochanter on the right side can be seen (Fig. 3).

## Discussion

Although ankylosing spondylitis may not uncommonly affect two or more members of the same family, e.g. two brothers or a brother and sister, its occurrence in two sisters is of sufficient rarity to be worthy of recording.

Both patients present some interesting features. Case 1, the subject of advanced ankylosing spondylitis, shows evidence of old healed rickets. The occurrence of the two diseases in the same patient is thought to be fortuitous, more particularly as there is a family history of rickets. In passing, I would like to record that I have seen another woman with a similar and more advanced combination of ankylosing spondylitis and old rickets.

Case 1 has well-marked mitral stenosis. It is not possible to establish whether this lesion has the same underlying aetiology as ankylosing spondylitis or whether it has been the result of a previous mild attack of rheumatic fever which has been overlooked. Hart and others (1949) found that the erythrocyte sedimentation rate was raised in the majority of their patients with ankylosing spondylitis, but

did not consider that the test was of much value in assessing the response to therapy. The findings in Case 1 tend to support this view, as the erythrocyte sedimentation rate has remained consistently high (40-50 mm.) in spite of obvious clinical and radiological improvement in the patient's condition. This patient also shows evidence of disease in the peripheral joints, especially the hip, shoulder, and temporo-mandibular joints. The latter have been extensively involved. Clinically there is recession of the lower jaw with marked limitation of movements of the mouth, while *x* ray reveals considerable loss of joint space. Erosion of bone at muscle attachment, which, according to some observers (McWhirter, 1945; Mowbray and others, 1949), differs in no way from the early subarticular erosions in the sacro-iliac joints, has been noted in ankylosing spondylitis. These lesions are present in Case 1 (Fig. 1) and affect notably the pubic rami, ischial tuberosities, the greater and lesser trochanters, and the lower cervical spinous processes.

The first symptom noted in Case 2 was pain down the back of both legs. Buckley (1945) laid great stress on the presence of sciatic pains as being among the earliest symptoms in ankylosing spondylitis, and showed that they may be present for as long as a year before there is any complaint referable to the sacro-iliac joints or spine, a point which cannot be stressed too often. Like her sister, this patient has evidence of peripheral joint involvement, affecting mainly the temporo-mandibular joints, the hips, and the hands. There is painful swelling of the proximal interphalangeal joints of the index and middle fingers, and a moderate degree of interosseal wasting, the appearances being clinically indistinguishable from rheumatoid arthritis. *X* ray of the hands shows soft-tissue swelling of the involved finger joints, and decalcification of the phalanges and metacarpal bones, but no loss of joint space. Case 2 also shows erosion of bone at muscle attachments, particularly at the right greater trochanter (Fig. 3), where calcification in the gluteus minimus has occurred. This osteoblastic invasion of muscle has been reported from time to time (Mowbray and others, 1949).

Finally, both patients complained of discomfort in the buttocks on sitting for any length of time and experienced considerable pain when pressure was applied over the ischial tuberosities. This is a not uncommon finding, but one that is liable to be overlooked.

**Summary**

(1) A brief review of the literature on the familial incidence of ankylosing spondylitis is given.

(2) Case records of two sisters with ankylosing spondylitis are presented. One of them is also the subject of old rickets.

(3) Some interesting features of the disease are brought out by a study of these patients.

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## Spondylite Ankylosante chez des Soeurs

RÉSUMÉ

(1) On passe brèvement en revue la littérature sur l'incidence familiale de la spondylite ankylosante.

(2) On présente l'histoire clinique de deux soeurs atteintes de spondylite ankylosante. Une d'elles avait des antécédents de rachitisme.

(3) L'étude de ces malades met en évidence quelques caractères intéressants de la maladie.

## Espondilitis Enquilosante en Hermanas

RESUMEN

(1) Reseñamos brevemente la literatura sobre la incidencia familiar de la espondilitis enquilosante.

(2) Señalamos la historia clínica de dos hermanas sufriendo de esta enfermedad. Una de ellas presentaba, además, síntomas de antiguo raquitismo.

(3) El estudio de estas enfermas pone en relieve algunos rasgos interesantes de esta enfermedad.

# A FURTHER ANATOMICAL CHECK ON THE ACCURACY OF INTRA-ARTICULAR HIP INJECTIONS IN RELATION TO THE THERAPY OF COXARTHRITIS

BY

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*London*

In an attempt to test the accuracy of the intra-articular injection treatment of coxarthritis, as used by Waugh (1945), Crowe (1944), and many other investigators; hip-joints of 33 cadavers were injected (Dobson, 1948) with dye solution which jellified on cooling. The technique of injection was similar to that applied in living patients undergoing treatment for osteo-arthritis of the hip. In 1947 at a Heberden Society meeting, D. P. Nicholson remarked on the difficulty of the procedure of injection into the arthritic hip-joint. He reported that in a series of 23 hip-joints radiographed after the intra-articular injection of diodone (an opaque dye) only one *x*-ray film confirmed the appearance of the dye in the joint injected (Nicholson, 1948).

It seemed that it might be of interest to record the results of a second series of forty hip-joints injected with the dye solution in the cadaver. Not only would an independent control be made on the original experiment, but a comparison could be made between the relative efficacy of the anterior and the lateral approach to the hip-joint.

## Material

In my second series of experiments on intra-articular injections in the cadaver, nearly all the bodies used were of good physique and weight, and were injected within a day or two of reception in the Anatomy Department. Thus a similar varied resilience of each tissue-substance penetrated by the needle was experienced, as in the living osteo-arthritic patient.

## Results

The results were recorded as positive when the dye was very plainly seen, inside the acetabular cavity, or on the head or intra-capsular part of the neck of the femur, or on the inner surface of the capsule lining. Only one example of a jell precipitate was seen in the outer capsular layers, and in the iliopsoas tendon in this series.

The results classed as negative imply an entire absence of any dye coloration inside or outside the capsule of the joint, or in the periarticular tissues. It may be presumed that the dye decolorizes or decomposes if in the softer tissues outside

the joint itself, or is intra-capsular rather than intra-articular. One grossly deformed osteo-arthritic hip was found on dissection. No dye was seen in this case, whether because of difficulty of penetration of the joint or not may be surmised.

At the end of 18 months the percentage of cases was found to be almost identical with that obtained in the previous series of hip-joints. An unfortunate over-concentration of carbolic acid used in the " curing " of seven bodies, prevented a consolidation of the dye as " jelly " in fourteen hip-joints injected, but the dye coloration was recognizable as such. The anterior approach to the joint resulted in a slightly higher proportion of successful results than the lateral approach; although both methods could give satisfactory results (see Table).

TABLE
COMPARATIVE RESULTS WITH LATERAL AND ANTERIOR APPROACH

| Results | Approach | |
|---|---|---|
| | Lateral | Anterior |
| Positive .. .. .. | 10 | 13 |
| Negative .. .. | 9 | 8 |
| Per cent. Positive .. | 52 (6) | 61 (9) |
| Total Cases .. .. | 19 | 21 |

Figs 1, 2, and 4, showing the acetabular cavity of three specimens, illustrate good positive results. The bright carmine jelly deposit (indicated by arrows) is seen right inside the cavity. Fig. 3 (rather distorted by foreshortening) demonstrates a similar deposition of jelly on the femoral head and inside the reflexion of capsule from the neck.

Thus it is reasonable to assume that 20 ml. fluid, injected by a similar technique into the hip-joint of the living patient, would bathe the articular components of the joint, and " swill out " the synovial membrane, fringes, and lining of the joint capsule.

## Summary

In forty cases of hip-injection in the cadaver, it was shown, by means of a special dye solution, that 67 per cent. were completely successful. In the former series of 33 cases, 61 per cent. had been successful.

The anterior method of approach to the hip joint may give better results than the lateral method, when intra-articular injections are attempted in osteo-arthritic patients receiving acid-injection treatment for coxarthritis.

Photographs of typical successful results emphasize the probable success in entering the hip-joint cavity in more than 60 per cent. of attempted intra-articular injections.

My thanks are due to Prof. Lucas Keene of the Anatomy Department of the Royal Free Hospital, London, for permission and encouragement to continue this work, and to Mr. Champion, the curator, for his valuable help in the preparation of the specimens.

FIG. 1.—Deposit in acetabular cavity of specimen A.

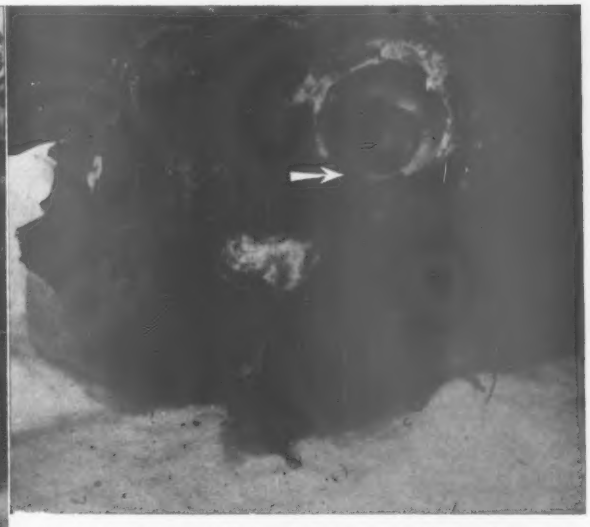

FIG. 2.—Deposit in acetabular cavity of specimen B.

FIG. 3.—Deposit on femoral head of specimen C.

FIG. 4.—Deposit in acetabular cavity of specimen D.

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## Nouvelles Vérifications Anatomiques de la Précision des Injections dans l'Articulation Coxo-fémorale, à propos du Traitement de l'Arthrite de la Hanche

RÉSUMÉ

L'injection d'un colorant spécial dans l'articulation coxo-fémorale des cadavres réussit complètement dans 67 pour cent des cas; il y eut 40 tentatives. Dans la série précédente de 33 tentatives, il y eut 61 pour cent de réussites.

La méthode d'accès antérieur à l'articulation de la hanche peut donner de meilleurs résultats que celle d'accès latéral dans le traitement de l'arthrite coxo-fémorale par des injections intra-articulaires d'acide.

Les photographies, montrant des résultats favorables typiques, mettent en relief les chances d'entrée dans la cavité articulaire coxo-fémorale dans plus de 60 pour cent des tentatives d'injection.

## Neuvas Comprobaciones Anatomicas de la Precision de las Inyecciones en la Articulation Coxo-femoral en Relacion con el Tratamiento de la Artritis de la Cadera

RESUMEN

Se notó un éxito completo en 67 por ciento de los 40 casos de inyección de un tinte especial en la articulación coxo-femoral de cadáveres. En la serie anterior de 33 casos el percentage de inyecciones logradas fué 61.

Al tratar la artritis coxo-femoral por inyecciones intra-articulares de ácido el método de acceso anterior a la articulación puede dar mejores resultados que el acceso lateral.

Las reproducciónes fotográficas, mostrando resultados favorables típicos, ponen en relieve la probabilidad de penetración de la cavidad articular coxo-femoral en más de 60 por ciento de tentativas de inyección.

# INVESTIGATIONS OF THE CREATINE EXCRETION IN THE URINE OF 38 UNTREATED AMBULANT MALE PATIENTS WITH FIBROSITIS, AND IN TWO HEALTHY MEN

BY

OLE SYLVEST and NIELS HVID-HANSEN

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When a patient with primary fibrositis* is examined, the diagnosis is made on the basis of the clinical examination because of the well-known fact that routine laboratory examinations all turn out negative. Therefore it was of great interest when creatinuria was detected in sciatica patients (Wang, 1939) and in patients with fibrositis (Brøchner-Mortensen and Clemmesen, 1941).

Wang examined, among other patients, ten with a not-further-defined sciatica; by means of 32 examinations in four men he found a creatinuria of from 0 to 215 mg. in 24 hours, with a total average excretion of 53·9 mg. in 24 hours, and by means of 106 examinations in six women values of from 0 to 620 mg. in 24 hours, with a total average excretion of 219·6 mg. in 24 hours.

Brøchner-Mortensen and Clemmesen's material consisted of twenty male patients with palpable muscular affections, nineteen of whom had creatinuria. The patients were hospitalized with fibrositis—chiefly in the lumbar and gluteal region; three of them also had sciatic neuritis. To some extent the creatinuria varied proportionally with the subjective and objective symptoms. The mean of the individual patients' average creatine excretion was 26·8 mg./kg. during 24 hours, which is a fairly considerable creatinuria.

Seeing, however, that by far the greatest number of patients with fibrositis are given ambulant treatment—because generally only patients with fairly severe muscular diseases are hospitalized—it must be of interest to try to find out how frequently creatinuria occurs among ambulant patients with fibrositis. In this way it may be decided whether this reaction should be introduced into physico-medical out-patients' departments as a routine laboratory examination.

According to most writers, creatinuria, as a rule, is not found in grown-up healthy males living on ordinary hospital diet (Brøchner-Mortensen, 1940). A few writers, however, do find a slight creatine excretion, but this very seldom exceeds 100 mg. per day (Horvath and Dill, 1941). In normal grown-up women an intermittent physiological creatinuria is often found in connexion with the period

* By fibrositis the investigators mean a localized area of increased consistency and tenderness in the musculature.

of menstruation and during pregnancy, especially in its last few months. The excretion in 24 hours is, however, usually less than 150 mg.

### Authors' Investigations

As material 38 male patients with fibrositis were examined. The patients were taken from the Physico-Medical Out-Patient Departments of the Co-operative Sick-Benefit Associations. They were diagnosed as cases of fibrositis by palpation by the specialists in physical medicine attached to the departments.

The creatine determinations were made by the authors by the following method :

Immediately after the first examination the patients are told to bring two specimens of urine (one from between 7 and 8 p.m., and one from the following morning). The specimens are preserved with 1 to 2 drops of toluene to hamper the growth of bacteria in the urine, and placed in a refrigerator. This, according to Horvath and Dill (1941), has no appreciable influence on the quantities of preformed and total creatine. The examination is carried out within 48 hours.

The creatine determination itself was made by means of the method described by Brøchner-Mortensen and Møller (1939), which again is a modification of Folin's method on the basis of Thomsen's work in 1938. We used Coleman's junior spectrophotometer for the colour-reading instead of Bürker's Pulfrich-Photometer.

The readings were taken at the wave length of 500 m$\mu$., a wave length chosen on the basis of the absorption spectrum for aqueous picric-acid solution, made basic ($p$H: 11·9) by means of NaOH, and a corresponding creatinine-containing solution respectively, choosing the wave length at which the difference between the extinction values of the above-mentioned solutions is greatest. In standard graphs made on the basis of the extinction values of well-known creatinine solutions, it is thus possible to determine the creatinine content of the specimens.

From the quantities thus found of preformed creatinine (without autoclaving) and of total creatinine (with autoclaving) an index is worked out, $\frac{\text{total creatinine} \times 100}{\text{preformed creatine}}$, which in creatine-free urine can vary from 95 to 105 (empirically calculated). If the index is greater than 105, the difference between total creatinine and preformed creatinine must represent the quantity of creatine; this can be worked out by multiplying the difference mentioned by 1·16 (obtained thus, $\frac{\text{molecular weight of creatine}}{\text{molecular weight of creatinine}} = \frac{131 \cdot 09}{113 \cdot 08} = 1 \cdot 16$). The content of creatine in the urine is then given in mg. per cent.

### Results

Among our 38 patients, aged from 16 to 68, we have found creatine excretion both in the urine collected in the evening and in that collected in the morning only in three. Two of those three patients had fibrositis in the lumbar and gluteal region, and the third patient in both arms. All three had had pain and probably also fibrositis for several years. These patients included a brewery worker of 42, a labourer of 39, and a factory manager of 22, who did a great deal of typewriting. Neither anamnestically, serologically, or clinically has any other explanation been found for the fairly large creatinuria which in these three patients ranged from 8·1 to 34·8 mg. per cent., with an average of 18·9 mg. per cent.

In four of the patients there was creatinuria in the evening urine only, which might be due to fibrositis, but was just as likely due to work, consumption of food (protein), drugs (e.g. preparations containing caffeine, see Bachmann, Haldi, Ensor, and Wynn, 1942), or other uncontrollable causes; it should be mentioned

that the excretion was small, except in a single case where it reached 54 mg. per cent. Finally, in one case there was a slight creatinuria in the morning only, which may probably be explained in the same way as the four last-mentioned cases.

All the patients had their urine tested for albumin, pus, blood, and sugar, and their blood for sedimentation rate, complement-fixation test for *N. gonorrhoeae*, Wassermann reaction, antistreptolysin titre, and haemoglobin per cent., and most of them also for agglutination reaction for haemolytic streptococci. All patients showed normal haemoglobin per cent. as well as negative complement-fixation test for *N. gonorrhoeae* and Wassermann reaction. In one patient we found sugar in the urine, but he had no creatine excretion in the urine, in the others we found no albumin, blood, pus, or sugar.

Sedimentation rate varied from 2 to 34; in the patients with creatine excretion in the urine both in the evening and in the morning, it did not exceed 6 mm. per hour.

Antistreptolysin titre varied from 0 to 160, and from 0 to 80 in those excreting creatine. The agglutination reaction for haemolytic streptococci varied from 0 to 1/160, and from 0 to 1/20 for those excreting creatine.

## Discussion and Conclusion

Two examinations for creatine were made of each patient, but as a creatine excretion lasting for 24 hours was found in only three out of the 38 patients, the conclusion may be drawn that determination of creatine in the urine is clinically of no diagnostic importance in ambulant male patients with fibrositis.

Since the palpation was performed by several examiners, who have all specialized in physical medicine, the physico-medical diagnoses may be looked upon as reliable.

From the investigation it is seen that creatinuria was detected in only 7·9 per cent. of a group of 38 ambulant male patients with fibrositis. The possibility cannot, of course, be excluded that more of the patients might be found to have creatine excretion in the urine if examined for a longer period. We have, however, desisted from this procedure, as it would make the diagnostic value of the method most problematic.

What is it then that determines the differences found in the material used in the two previous investigations as against our results? Several circumstances must be taken into account:

(1) Our material consisted of patients who were untreated when examined, unlike Brøchner-Mortensen and Clemmesen's, who had nearly all been given thermotherapy or massage. Massage especially may be expected to have an injurious effect on the musculature, thus leading to creatine excretion. Against this, however, is the fact that Brøchner-Mortensen and Clemmesen's patients showed some congruity between the variations of the excreted amount of creatine and the clinical condition, in spite of the fact that massage was carried on in some of the cases. In order to investigate the matter more closely, if possible, we had two healthy men with no muscular diseases massaged, one was given universal

massage for one hour once, the other had his gluteal region and lower limbs massaged hard for half an hour every day for a week; in neither of those cases was creatinuria detected, either during the period of treatment or during the following 48 hours.

(2) The material of Wang, and of Brøchner-Mortensen and Clemmesen, consisted of hospitalized patients in contrast to our ambulant patients. Thus it might be thought that a period in bed which in itself causes atrophy of the muscles, would also cause creatinuria. Our first experiment also pointed in that direction: in a patient sent to hospital with fracture of the skull and concussion after a road accident, after three days and nights of creatine-free urine we found a heavy creatinuria ranging from 444 to 139 mg. per 24 hours, continuing for thirteen days and nights with an average creatine excretion of 230 mg. per 24 hours. This creatinuria decreased as the patient improved, and the creatine excretion stopped several days before the patient began to be less strictly confined to bed. Experiments on two grown-up, healthy men, kept strictly in bed for a week, showed no creatinuria whatsoever in spite of the fact that they kept commendably quiet. These results with the two healthy men agree with those of Deitrick, Whedon, and Shorr (1948) in healthy men confined to bed in plaster casts. By experiments with administration of creatine those investigators also found that if the patients do not keep to their beds almost all the creatine administered is retained, whereas a great deal is excreted if they are put into plaster casts.

Therefore we should be justified in leaving staying in bed and massage out of account as causes of creatinuria in patients on an ordinary hospital diet. The difference between the results with Brøchner-Mortensen and Clemmesen's hospitalized patients and our ambulant patients was probably quantitative, since the hospitalized patients were probably suffering from a much more pronounced fibrositis than our ambulant patients. This idea is also supported by the fact that our three patients with a 24-hour creatinuria seem to have been among the most heavily afflicted patients in our material—having, for instance, suffered from the disease for several years.

On the basis of our investigations we cannot therefore recommend examination for creatinuria as a guide in the diagnosis of fibrositis in ambulant male patients.

## Summary

Examining 38 ambulant, partly working, male patients with fibrositis, we found creatinuria in the evening as well as in the morning in three (7·9 per cent.) all of whom had had symptoms for several years, and a slight creatinuria in five (13·2 per cent.), i.e. in the evening only in four, and in the morning only in one (which may probably be explained in some other way).

A week's massage or staying in bed caused no creatinuria in two healthy men.

We wish to thank the chief physicians of the Out-patient Department, Drs. Kjer, Krogh-Lund, Pontoppidan, Walter, and Wieth-Petersen, for permission to use these 38 patients as material. The spectrophotometer apparatus was kindly put at our disposal by the University Medico-physiological Institute. The work was supported by a grant from the National Danish Association against Rheumatic Disease.

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**Investigations de l'Excrétion Urinaire de la Créatine chez 38 Malades Ambulants, Non-Traités, Mâles, atteints de Fibrosite, ainsi que chez deux Hommes Sains**

RÉSUMÉ

A l'examen de 38 malades ambulants, mâles, partiellement occupés, atteints de fibrosite, on a trouvé que trois d'entre eux (7·9%), dont les symptômes remontaient à plusieurs années, présentaient de la créatinurie matin et soir; chez cinq (13·2%) la créatinurie fut trouvée une fois chaque jour: chez quatre le soir et chez un le matin seulement (chez ce dernier probablement pour une raison différente).

Une semaine de massage ou d'alitement chez deux hommes normaux ne provoqua pas de créatinurie.

**Investigacion de la Excrecion Urinaria de la Creatina en 38 Enfermos Ambulantes, No Tratados, con Fibrositis, Asi Como en dos Hombres Sanos**

RESUMEN

Al examinar 38 enfermos con fibrositis, ambulantes, trabajando parcialmente, hemos encontrado que tres de ellos (7·9%) con síntomas desde muchos años, mostraban creatinuria por la mañana y por la noche; en cinco (13·2%) hubo creatinuria una vez al día: en cuatro por la noche y en uno por la mañana solamente (en el último probablemente por una razón diferente).

Una semana de masage y de reposo en cama no provocó creatinuria en dos hombres sanos.

# HEBERDEN SOCIETY

## HEBERDEN ORATION*

Professor Hans Selye, Director of the Institute of Experimental Medicine and Surgery in the University of Montreal, delivered the Heberden Oration at B.M.A. House, London, on June 2 and 3, 1950. His subject was " Stress and the General Adaptation Syndrome ". The President, Dr. W. S. C. Copeman, was in the chair.

Prof. Selye began with the apology that much of what he had to say could only be vague, but said that a preliminary map of a country, even though incomplete and in some respects inaccurate, was a useful possession. In this sense he turned to the principal facts and theories upon which the general adaptation syndrome concept was based. The general adaptation syndrome (G.A.S.) was an integrated syndrome of closely interrelated adaptive reactions to non-specific stress. It developed in three stages: the alarm reaction, the stage of resistance, and the stage of exhaustion. Most of the characteristic manifestations of the alarm reaction, such as tissue catabolism, hypoglycaemia, gastrointestinal erosions, disappeared or were reversed during the stage of resistance, but reappeared in the stage of exhaustion.

In G.A.S. the manifestations of passive non-specific damage were intricately intermixed with those of active defence. In the biological sense, stress was the interaction between damage and defence. In addition to damage and defence, every stressor also produced certain specific actions—anaesthetics, for example, acted upon the nervous system, diuretics upon water metabolism, insulin upon blood sugar—quite apart from their stressor effects. Hence the general adaptation syndrome never occurred in its pure form, but was always complicated by superimposed specific actions of the eliciting stressors.

**The Nervous Defence Mechanism.**—Nervous impulses descended from the hypothalamic vegetative centres, through the autonomic nerves, to the peripheral organs. The splanchnics induced the adrenal medulla to discharge adrenergic hormones into the blood. Presumably this discharge was most effective when the adrenergic hormones were needed throughout the body, while the sympathetic nerves were better suited to impart similar impulses selectively to certain circumscribed territories. The most conspicuous results of such neuro-humoral discharges were changes in the contractility of smooth muscle. Owing to an adrenergic vasoconstriction, peripheral resistance increased and blood pressure rose. This hypertensive response might be further accentuated by an increased cardiac volume and the opening of the renal shunt which deviated blood from the cortical glomeruli to the juxtamedullary region of the kidney.

The principal endocrine response to stress was characterized by the so-called shift in anterior-lobe hormone production, consisting in a diminished secretion of somatotrophin, the gonadotrophins, and thyrotrophin, accompanied by an increase in the secretion of ACTH. This last was a " gluco-corticotrophic " hormone, which induced the adrenal cortex to produce predominantly gluco-corticoids, as, for example, " compound F ", cortisone. The latter acted upon the blood count, the thymico-lymphatic tissue, the reticulo-endothelial system, and gluconeogenesis. The gluco-corticoids presumably influenced resistance in many additional ways not yet fully analysed. All gluco-corticoids so far examined possessed some mineralo-corticoid activity. Their action upon the kidney had not yet been extensively studied, but preliminary investigations showed that they caused marked hyperaemia of the glomeruli and might render the latter impermeable to proteins and even to blood. They inhibited the production of

* The first part of Prof. Hans Selye's oration appeared in full in the *Brit. med. J.* (1950), **1**, 1383, and a synopsis of the second part in (1950), **1**, 1362.

arteriosclerotic changes, generally inhibited excessive proliferation of fibrous tissue, and through their effect upon the blood proteins also tended to decrease the erythrocyte sedimentation rate, acting in all these respects as antagonists of the mineralo-corticoids.

Prof. Selye discussed at some length the mutually antagonistic action of the gluco-corticoids and the mineralo-corticoids, and the action of both types of corticoids upon the anterior lobe, both of them inhibiting its ACTH production through the so-called phenomenon of " compensatory atrophy ".

**Diseases of Adaptation.**—The polymorphism of the G.A.S. symptomatology was thus due to two principal reasons. First, every stressor had specific actions in addition to its stress-producing ability. The former modified the response caused by stress as such; hence the polymorphism of the G.A.S. manifestations could be due to specific effects of the evocative stressors. But even exposure to the same stressor agent might result in qualitatively different responses. Here polymorphism of the G.A.S. manifestations was due to selective conditioning by factors extraneous to the stressor. This peripheral conditioning might occur at the various intermediate stations of the G.A.S. or in the target organs themselves. The closer the periphery was approached the more often were deviations from the standard general adaptation syndrome pattern to be noted.

It might be asked why diseases of adaptation were so polymorphic in their manifestations if they were all due to stress. The principal reasons were the so-called conditioning factors just mentioned, namely, the specific effects of the evocative stressors and other exogenous or endogenous factors which could affect, selectively, certain pathways or target organs of the G.A.S. response.

A further question was why exposure to the same stressor should produce disease only in certain individuals. The G.A.S. was a useful, normal physiological reaction to stress; only its derailments had been interpreted as diseases of adaptation. Hence exposure to a stressor could be expected to produce such diseases only if the defence reaction was inadequate. A number of other criticisms of the G.A.S. concept had also to be dealt with. One of the most common questions asked was how the two facts could be reconciled that the " rheumatic-allergic " type of disease was produced by corticoids in animals and nevertheless responded so favourably to corticoid therapy in man. The answer was that the original animal experiments of necessity had to be performed with a mineralo-corticoid, since this was the only adrenal steroid available in adequate amounts, and its effects upon many target organs were the reverse of those produced by gluco-corticoids (e.g. cortisone). This was due partly to a peripheral antagonism at the level of the target organs themselves, and partly, perhaps, also to the inhibition by gluco-corticoids of mineralo-corticoid production through the " compensatory atrophy " phenomenon.

**Therapeutic Measures.**—It was becoming increasingly evident that many of the time-honoured non-specific therapeutic measures, such as fever-therapy, shock-therapy, blood-letting, or mere starvation, were beneficial largely through the G.A.S. Often their principal value appeared to be that they stimulated ACTH and gluco-corticoid production. Wherever this was so it might be preferable in the future to inject ACTH or cortisone, though in certain instances non-specific therapy proved efficacious where ACTH failed.

Assessing the scope (so far as this was possible in view of the limited amounts available) of the clinical use of ACTH and cortisone, Prof. Selye gave a list of some fifty conditions in which these hormones had been shown to be of value. They included various allergies, eczema, fevers (apparently irrespective of aetiology), gouty and rheumatoid arthritis, Hodgkin's disease, leukaemias (various), ophthalmological conditions, psoriasis, serum sickness, and ulcerative colitis. There were a number of other conditions, such as glaucoma, myasthenia gravis, and scleroderma, in which this type of treatment might also be of value. In certain conditions, such as diabetes mellitus and poliomyelitis,

available data suggested that the treatment was of no value; in a number of others, such as acne vulgaris, osteoporosis, and peritonitis, it might produce harmful effects; and in certain others, it might actually cause marked decrease in resistance to infections, obscure the criteria of disease, or even produce acute pulmonary oedema and ascites.

**Problems for Future Research.**—In concluding the first part of his oration Prof. Selye indicated certain lines of future research:

(1) The problem of the " first mediator ". More information was required concerning the stimuli which, during stress, induced the pituitary to discharge ACTH.

(2) The possible therapeutic value of general adaptation syndrome components, other than adrenalin, ACTH, and gluco-corticoids. It was highly probable that many other manifestations of G.A.S. participated in raising resistance.

(3) The degree of correlation between gluco-corticoid and anti-arthritic activity. The further elucidation of certain aspects of steroid pharmacology would extend the scope of pharmaco-therapy in the diseases of adaptation.

(4) The degree of correlation between mineralo-corticoid and hyalinosis activity. There was need for a more profound analysis of this correlation.

(5) The scope of the activities of " conditioning factors " (diet, drugs, etc.) which selectively increased or decreased the action of stress hormones upon certain organs.

(6) The selective conditioning of the adrenal response. The possibility of influencing the adrenal to produce different kinds of hormones at will deserved special mention.

(7) The problem of selective hypocorticoidism, or the relationship between complete hypocorticoidism, as caused by adrenalectomy, and selective hypo-glucocorticoidism, as induced by mineralo-corticoid overdosage.

(8) The explanation of the observation that the conditions which caused the kidney to produce an excess of renal pressor substances also interfered with its ability to detoxify such pressor substances.

(9) The ability of ACTH or cortisone to produce remissions in both granulocytic anaemias and agranulocytosis.

(10) The reason, if any, for the similarity in the pharmacological effects of adrenergic and corticoid compounds.

Disease consisted of two components: damage and defence. Medicine had so far attempted to attack only the damaging pathogen, and defence had been limited to vague advice about rest or food. A study of the general adaptation syndrome suggested that henceforth it would be possible to aid adaptation to non-specific local or systemic injury by supplementing the natural defensive measures of the general adaptation syndrome whenever these were suboptimal.

**The Clinical Application.**—In the second part of his oration Prof. Selye dealt with the clinical applicability of the concept which he had advanced. He said that such clinical demonstrations were possible because of the great work of the organic chemists who had furnished the essential hormones, and he mentioned in particular the work of Kendall and Li, as well as that of clinicians such as Hench.

By means of comparative photographs he showed the rapid clinical improvement and even cure effected in a wide range of cases, largely of rheumatic type, by the use of cortisone or ACTH. He began with rheumatoid arthritis of the elbow joint. In one such case, within four days of ACTH administration, the relaxation of the joint was such as to permit of the normal raising of the arm, which had before been very restricted. In another case of rheumatoid arthritis with swollen fingers there was marked regression within five days of administration of ACTH. He exhibited next a case of lupus erythematosus, with butterfly rash on the face, high fever, and extremely rapid sedimentation rate. Within a few weeks after ACTH had been given (in divided doses several times a day) the face and the sedimentation rate were completely normal, and the fever had subsided. This patient developed Cushing's disease, with vascular hypertension, hirsutism,

adiposity, and osteoporosis, but when ACTH administration was stopped these manifestations disappeared and the lupus did not recur. In a bad case of psoriasis, the granuloma became acellular and starlike within a few days of treatment with cortisone, and eventually there was complete healing. In gout an attack might be precipitated as well as prevented by ACTH. Large doses might bring about an attack in a predisposed person, but smaller and more gradual doses depleted the body of its uric acid store and forestalled attacks. A case of severe rheumatic pancarditis cleared up under large doses of cortisone. Here attention was drawn to the fact that until a water-soluble cortisone was available—which might be within the next year—ACTH was the more rapidly acting drug.

**Eye Conditions.**—The availability of cortisone was a big problem, and when only small amounts were obtainable, preference should be given to those cases in which complications were most likely to occur if the disease were left alone. This applied especially to eye diseases, which, if untreated, might lead to blindness. Cortisone acted locally and could be injected under the conjunctiva or used as an eye ointment. Thus only 2 mg. cortisone might save a patient's eyesight, whereas 80 mg. might do little good in a case of rheumatoid arthritis.

Many of the acute inflammations of the eye were often referred to as of the rheumatic type, which from a morphological point of view was difficult to separate from the allergic type. Many such cases could be dramatically improved and in some cases brilliantly cured by ACTH or cortisone therapy. He gave a typical example of conjunctivitis vernalis which became almost normal within 48 hours, and was completely normal a few days later. A case of herpes zoster of the eye in a woman aged 64 cleared up within four days of cortisone administration. A case of fulminating hypopyon—a colour photograph showed how cloudy was the anterior chamber—showed a recession of the hyperaemia with absorption of all the keratinization except for a thin film two days after the administration of cortisone. A case of specific choroiditis cleared up after three days.

**Back to the Theory.**—After discussing the side effects—the Cushing manifestation, the possible aggravation of renal changes, osteoporosis, and other complications which he said were rare and he believed would be overcome—Prof. Selye turned in conclusion to the fundamental objection to the theory, namely, that the same pathogen could not cause such a multiplicity of diseases in man, and that surely every disease must have its own separate cause. In the days before the problem of tuberculosis had been worked out, a group of physicians might have felt a similar scepticism if they had been told that the same pathogen was responsible for such a multitude of manifestations, in the lungs, bones, skin, kidneys, and many organs and tissues. It was not an unreasonable conjecture that a wide variety of diseases now regarded as of unknown origin were in fact diseases of the adaptation syndrome.

" The only purpose of a theory in medicine is to act as a line of guidance and to lead to the elucidation of important new facts. I think I can safely say that the facts which I have reported are correct. Whether the theories will be useful, only their application to medicine will be able to show."

Votes of thanks were proposed to the Orator by Lord Moran and Sir Henry Cohen.

## HEBERDEN ROUND, PARIS, 1950

The Heberden Round was given by Prof. F. Coste, Professor of Rheumatology in the University of Paris, at the Hôpital Cochin, Paris, on May 20 and 21, 1950, and members of Professor Coste's unit and his associates took part in the presentation of cases and short papers. The President, Dr. W. S. C. Copeman, was in the chair. Many members of the French branch of the Ligue Internationale contre

le Rhumatisme attended, and members of the British branch were also invited. The following cases and papers were presented:

(1) *Dr. S. Brion* showed a case of carcinoma of the prostate, with multiple secondaries, involving D.9, who had developed a paraplegia. The patient had been treated with large doses of oestrogens with partial recovery.

(2) *Drs. F. Delbarre, M. Bourel, and J. Hinaut-Oury* presented three cases of multiple myeloma:

  (*a*) A man of 24 treated with aureomycin with some clinical response but subsequent relapse.

  (*b*) A man of 50 with lumbar pain treated with aureomycin without effect, who finally developed a paraplegia. The erythrocyte sedimentation rate rose from 23 to 63 mm. during treatment.

  (*c*) A female aged 66 with diffuse decalcification, showing 17 per cent. plasmacytes in the marrow and greatly raised gamma globulin, showing little improvement on similar treatment.

(3) *Dr. F. Delbarre* reviewed the forty cases of myelomatosis seen at the Hôpital Cochin during the last 3 years. Diagnostic pointers included a high erythrocyte sedimentation rate and hyperproteinaemia; the Formol-gel test had also been found useful since Kala-azar is extremely rare in France. Treatment with aureomycin had been tried, on the hypothesis that the condition might be a virus infection, but the results had been disappointing except for one case which seemed to show some response.

(4) *Dr. J. P. Amoudruz* read a paper on the use of tomography in the study of changes in the sacro-iliac joints in ankylosing spondylitis. This technique appeared to be useful in showing changes at an early stage before they were apparent on a straight view.

(5) *Prof. F. Coste and Dr. S. Brion* presented a case of polyostotic fibrous dysplasia (Jaffé-Lichtenstein syndrome) with gigantism, acromegaly, and late puberty in a woman of 23.

(6) *Prof. F. Coste and Mme. Lacronique* showed a case of a man presenting with pain in the shoulder and neck with an opacity apparent on *x* ray of the chest, localized by tomography as lying in the second rib. This was considered to be a metastatic deposit. The primary was localized in the bladder but the histology was not identified for technical reasons. He was treated with deep *x* ray to both lesions with some relief.

(7) *Prof. F. Coste and Dr. Amoudruz* showed a case of a man aged 59 with severe osteo-arthritis of the left hip joint which prevented him carrying out his work or walking more than a few yards. He was treated with lateral differential cordotomy on the right side at the level of C.1-2 under local anaesthesia with very carefully controlled cutting of fibres and entire disappearance of pain. There was also some loss of temperature sense over the left thigh, but he was able to walk quite well.

(8) A film illustrating the effects of ACTH in cases of rheumatoid arthritis was shown by Dr. F. Delbarre, Dr. G. Basset, and Dr. G. Georges. Dr. Delbarre described cases treated with an active preparation of ACTH made in France; his paper entitled " Étude d'une cortico-stimuline hypophysaire " will appear in the next issue of this journal.

(9) *Dr. M. Bourel* gave an account of experimental and clinical work on the permeability of the synovium by means of the perfusion of saline and other agents through the synovium of rabbit's knees. Hyaluronidase increased the speed

but heparin and histamine had little effect. Of twelve patients treated with hyaluronidase introduced into the knee joint, nine showed temporary improvement only, and it was concluded that there was no practical benefit.

(10) *Prof. Merle D'Aubigné* discussed the surgical treatment of spondylolisthesis. He gave the indications for surgery as being severe pain, failure of exercises or supports to the back, and sciatica. The objects of operation were threefold: reduction, fixation, and the freeing of affected nerve roots. An anterior operative approach was ideal for reduction and fixation, and a posterior approach enabled the nerve roots to be freed and good fixation to be obtained. Sciatica was therefore an indication for a posterior approach. A film was shown of the operative technique.

(11) *Prof. F. Coste and Mme. Lacronique* surveyed their attempts to stimulate the pituitary and adrenal glands by various physical and chemical methods. This paper will be printed in full in the next issue of this Journal.

(12) *Dr. E. G. L. Bywaters* read a paper on post-rheumatic arthrosis of the type first described in the *Revue de Rhumatisme* by Jaccoud in 1869. It was recognized in England up to the end of the nineteenth century, but was not generally known in America or England, although French authors had described such cases recently. A case was described which also showed radiological changes not thought to be those of rheumatoid arthritis. Search through a post-mortem series showed other cases probably similar in nature. The Jaccoud syndrome must be distinguished from cases of rheumatoid arthritis with rheumatic heart disease and from rheumatoid arthritis cases who had rheumatic fever in childhood with residual cardiac lesions. The pathology of the condition was thought to be mainly a fibrosis and as such seemed to be resistant to adrenocorticotrophic hormone. This paper is to appear in a forthcoming issue of the *Revue de Rhumatisme*.

(13) *Dr. J. Forestier and Dr. J. Rotes* presented a paper on ankylosing vertebral hyperostosis of old age which will be printed in full in the next issue of this Journal.

(14) *Dr. Mathieu Pierre-Weil and Dr. Sichère* discussed anginal symptoms occurring during rheumatoid arthritis and described four cases where anginal pain developed during the disease, the pain being severe enough to suggest a myocardial infarct. At the same time, the prognosis appeared good and electrocardiogram changes slight.

(15) *Dr. G. D. Kersley* presented an account of a case of gout with post-mortem findings. This will be printed in full in the next issue of this Journal.

(16) *Prof. A. S. de Sèze* showed an excellent film used in teaching radiographic methods with reference to the spine.

(17) *Prof. A. Thiers* showed an unusual case of Reiter's syndrome.

(18) *Dr. F. Layani* showed a case of carcinoma of the breast with multiple bone deposits revealed by a spontaneous fracture of the fibula. This was treated with large doses of androgens with radiological improvement and the patient was clinically free from symptoms when demonstrated. A case of shoulder-hand syndrome of Steinbrocher treated with stellate block with procaine with some improvement was also demonstrated.

Also, *Dr. J. A. Lièvre* was to have presented a paper on the significance of acute lumbago, but time was too short for it to be read at the meeting and an account is to be published in the *Revue de Rhumatisme*.

# NEW YORK ACADEMY OF MEDICINE

A Symposium on the Present Status of Cortisone and ACTH was presented on January 12, 1950, at a special meeting arranged by the Committee on Medical Education under the chairmanship of Dr. R. F. Loeb. The seven papers abstracted below were published in full in the *Bulletin of the New York Academy of Medicine* (1950), 2nd Series, Vol. 26, No. 4.

**Effects of Cortisone and ACTH in Rheumatoid Arthritis.** By R. H. Freyberg.

The author reviews the effects of treating 169 cases of chronic rheumatic disease with cortisone and 175 with ACTH (the total so far treated in America). Cortisone and ACTH are effective in the treatment of rheumatoid arthritis, rheumatoid spondylitis, Still's disease, and psoriasis with arthritis. The average dosage for cortisone is 100 mg. daily, in one injection, until a remission is induced, and then 100 mg. thrice weekly. With ACTH it seems preferable to give small doses (generally 25 mg. of standard preparation) four times daily. Relapse after cessation of treatment usually occurs rapidly. Complications include: oedema from sodium retention, hypopotassiumaemia, partial hypercortico-adrenalism, menstrual disorders, diabetic carbohydrate metabolism, insomnia, tachycardia, excitability, and mental depression. They occur more frequently in women, particularly those of premenopausal age, and in children, who require comparatively larger doses.

Substances chemically similar to cortisone studied to date, include compound S, progesterone, 17-hydroxyprogesterone, pregnenolone, acetoxy-pregnenolone and testosterone, but all are ineffective. In conclusion it is emphasized that, since prolonged administration of cortisone may lead to adrenal atrophy and that of ACTH to pituitary atrophy with adrenal hyperplasia, further research on this problem is required before the hormones can be considered for practical therapy. It remains, however, the greatest advance in the treatment of rheumatic diseases.

**The Effect of Cortisone and ACTH on Rheumatic Fever.** By C. McEwen, J. J. Bunim, J. S. Baldwin, A. G. Kuttner, S. B. Appel, and A. J. Kaltman.

The results of cortisone and ACTH therapy in three children with acute rheumatic fever are described, and the authors also summarize the current literature on the subject. It is confirmed that fever, polyarthritis, " rheumatic toxicity ", and nodules, responded rapidly to treatment with either cortisone or ACTH. The sedimentation rate, leucocyte count, and haemoglobin concentration, returned more slowly towards normal, and a slight rise in serum albumin with a fall in the globulin was noted. Pericardial friction rubs and atrioventricular conduction defects cleared rapidly but may improve spontaneously. Complications included salt- and water-retention, transient hypertension, glycosuria, mental disturbances, hypocalcaemia, a peculiar facial eruption, and some features of Cushing's syndrome. The effect of the therapy on the carditis was more difficult to assess and the authors conclude that further study of a larger number of cases with carditis is necessary before the value of cortisone and ACTH in this condition can be assessed.

**The Treatment of Disseminated Lupus Erythematosus with Cortisone and Adrenocorticotropin.** By G. Baehr and L. J. Soffer.

The results of treating five cases of disseminated lupus erythematosus (four women, and one boy of 13 years) are discussed. It was found that the optimum dosage was 150-200 mg. cortisone, or 100 mg. ACTH, given daily in four divided doses. When the rash

and other signs of the disease had disappeared the dose was reduced to 50-100 mg. cortisone, or 75-100 mg. ACTH. In order to stimulate adrenal cortical activity cortisone was replaced by ACTH as soon as the maintenance dose of cortisone had been determined. The amount of ACTH was then gradually reduced over 4 to 6 weeks until the patients' own adrenals assumed the full load.

Complications included sodium retention, hypertension, hypopotassiumaemia, and cerebral disturbances. Details of treatment of these conditions are given. Improvement was dramatic in all cases, but it is stressed that the therapy must be considered as producing a remission and not as a curative procedure, since leucopenia, raised sedimentation rate, and the presence of " L.E." cells in the bone marrow, persisted after apparent clinical recovery.

**The Use of ACTH and Cortisone in Neoplastic Disease.** By O. H. Pearson, L. P. Eliel, and T. R. Talbot, Jr.

Five cases of acute leukaemia (one lymphocytic and four granulocytic) were treated with ACTH, in doses of 50 mg. daily for children and 100 mg. daily for adults. In all cases there was a dramatic improvement, with rapid shrinkage of spleen, liver, and lymph nodes, and some improvement in the blood picture as shown by increased maturity of circulating leucocytes and marked reticulocytosis. Similar improvement was seen in the bone marrow, but in no case did the blood or bone marrow return to normal, and in one case a relapse occurred three weeks after discontinuing ACTH.

Two cases of acute leukaemia which had previously received antifolic treatment died after beginning ACTH therapy, but both were already critically ill. One case each of carcinoma of the breast, embryonal carcinoma of the testis or adrenal, Ewing's tumour, plasma cell myoma, rhabdomyosarcoma, and carcinoma of the pancreas, showed no definite response to ACTH.

The authors have little experience of the use of cortisone in acute leukaemia, but one child showed a good remission whereas another died 48 hours after starting cortisone therapy. It is concluded that ACTH can produce remissions in cases of acute leukaemia but is not curative.

**Physiology of the Pituitary-Adrenal System.** By Jane A. Russell.

In reviewing the chemical composition of the known adrenal steroids, the author points out that the six or seven hormones which are active in maintaining life in adrenalectomized animals may be divided into those oxygenated at the 11-carbon atom and those not so oxygenated (desoxy type). Cortisone (compound B) and 11-dehydrocorticosterone (compound A) are less active than 17-OH, 11-dehydrocorticosterone (compound E or cortisone); the most potent, but the most difficult to synthesize, is 17-OH corticosterone (compound F).

The physiological effects of these hormones are described as follows:

(1) Maintenance of salt and water balance is demonstrable since lack of the hormones gives rise to salt depletion, dehydration, and rise in the plasma potassium, whereas overdosage, as in treatment with cortisone, may lead to salt-retention and oedema.

(2) Lack of corticosterones gives rise to increased nitrogen loss and depletion of muscle glycogen, the site of action probably being on some phase of gluconeogenesis from body protein. Excess hormone therapy has also a diabetogenic effect, the desoxy compounds being less active in this respect.

(3) Involution in lymphoid tissue and decrease in circulating eosinophils occur in hormone deficiency and the hormones also appear to affect the spreading factor in the skin, probably by inhibition of hyaluronidase.

(4) Resistance to stress and adaptation to environmental change is diminished by hormone lack, particularly by lack of the 11-oxygenated steroids, although the mode of action is unknown in this respect.

Experimentally ACTH has the same effect as the corticosteroids, but functioning adrenal tissue is necessary for its effective action. It has also been shown that the adrenals are practically inactive in the absence of pituitary secretion.

**The Effect of ACTH and Cortisone on Connective Tissue.** By C. Ragan, E. L. Howes, C. M. Plotz, K. Meyer, J. W. Blunt, and R. Lattes.

The authors give a brief account of experiments to show the effect of cortisone and ACTH on wound healing. Skin defects were made in the ears of one series of rabbits by the Howes method, and femoral fractures were made in a second series by the Hudack and Blunt technique.

It was found that there was marked delay in wound healing and fibroblast reaction in the animals previously treated with ACTH or cortisone compared with the controls. Large doses of cortisone, equivalent to 500 mg. daily in a 50-kg. adult, seemed completely to suppress granulation-tissue formation, whereas smaller doses merely delayed its appearance.

It is suggested that the hyperadrenal state renders the mesenchymal tissues incapable of reacting to trauma from whatever cause, and that this may be the reason for a similarity in remission of symptoms in clinically different diseases treated with ACTH or cortisone.

**The Relationship of Adrenal Cortical Activity to Immune Responses.** By E. E. Fischel.

A series of experiments is described to show the effect of ACTH and cortisone on the development of immune or allergic reactions, and the findings of other workers on similar experiments are discussed.

Using Kabat's quantitative technique for the induction of anaphylaxis, it was found that the response of guinea-pigs was unaffected by treatment with ACTH. The Arthus reaction was used for a quantitative study in rabbits and guinea-pigs, but there was no appreciable difference in reaction between controls and ACTH-treated animals. The anamnaestic response was studied in rabbits using crystalline egg albumin, but no rise occurred in the antibody content of the serum of animals treated with ACTH. Finally, hyperglobulinaemia was produced in rabbits by a pneumococcal immunization technique, and it was apparent that antibody formation was significantly diminished in ACTH-treated animals.

It is concluded that ACTH and cortisone do not alter the union of antigen and antibody but may have some effect on the formation of antibody. Further study is recommended.

# WORLD HEALTH ORGANIZATION

## THIRD ASSEMBLY

### LIGUE INTERNATIONALE CONTRE LE RHUMATISME

At its session on May 18, 1950, the Programme Committee of the W.H.O. adopted the following resolution:

**Rheumatic Diseases.**—The Programme Committee of the Third World Health Assembly adopts the following resolution:

That the Third World Health Assembly appreciates the importance of the social and economic problems which are a result of the frequency of the rheumatic diseases and decides to:

(1) RECOMMEND that the Executive Board and the Director-General when determining the programme and budget for 1952, make the appropriate provisions for the establishment of an Expert Committee to deal with the rheumatic diseases and their necessary remedies.

(2) REFER the suggestions contained in the document A3/Prog/13 to the proposed Expert Committee.

(3) SUGGEST to the Director-General to assist by all means possible the governments desirous of undertaking the investigations into this problem.

### STATEMENT BY PROF. DR. KARL M. WALTHARD, GENEVA,

*Representative of the Ligue Internationale contre le Rhumatisme*

"On behalf of the Ligue Internationale contre le Rhumatisme I should like to express gratitude to the Danish Government delegation for its proposal to set up an Expert Committee, and to the French Government delegation for its memorandum bringing attention to the grave problems of the rheumatic diseases. It is not my intention here in detail to go into the very intricate consequences of the rheumatic diseases, but I must in particular underline the existence of the very heavy economic burdens which the rheumatic diseases place on the many countries in which a very great number of persons have for many years past been invalided by these afflictions.

"The Ligue Internationale contre le Rhumatisme endeavours to co-ordinate the total scientific efforts to combat the rheumatic diseases, but it is important in order to achieve this object to obtain the aid of the World Health Organization."

A3/Prog/5 and 13

*Session, May* 18, 1950, 4.15 *p.m.*

# LIGUE EUROPÉENNE CONTRE LE RHUMATISME

### EXTRACT FROM THE DIRECTORY OF INTERNATIONAL SCIENTIFIC ORGANIZATIONS

2. *Address:* Headquarters of the Secretariat: St. Strandstraede 19, Copenhagen K, Denmark.
3. *Nature:* Non-governmental.

4. *Aims:* To co-ordinate all research and the treatment of rheumatic complaints initiated by scientific and social organizations in the member countries of the Ligue.

5. *Governing Bodies:* The supreme authority of the Ligue is the Council, which elects the president of the Ligue Européenne and two vice-presidents. The president is appointed for two years and is not eligible for re-election. The officers consist of the president of the European League and former president, the two vice-presidents and members of the secretariat-general, in addition to the president and secretary-treasurer of the Ligue Internationale contre le Rhumatisme.
Officers: President: Dr. W. S. C. Copeman (U.K.); 1st Vice-President: Dr. M. Ferond (Belgium); 2nd Vice-President: Dr. Pedro Barcelo (Spain); Past-President: Dr. Mathieu Pierre-Weil (France); Secretary-General: Professor Gunnar Edström (Sweden); Treasurer: Mr. Ove de Bornemann (Denmark); Secretary: Dr. K. Kalbak (Denmark); President of Ligue Internationale contre le Rhumatisme: Professor Dr. E. Jarløv (Denmark); Secretary-Treasurer to Ligue Internationale: Dr. W. S. Tegner (U.K.).

6. *Members:* Each member country elects and delegates one representative and one deputy representative to the Ligue. They are appointed for a term of four years and are eligible for immediate re-election. The following countries are members: Austria, Belgium, Czechoslovakia, Denmark, Eire, Finland, France, Hungary, Italy, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, Turkey, United Kingdom, Yugoslavia.

9. *Finances:* A percentage of the total annual subscriptions is paid to the Ligue Internationale contre le Rhumatisme.

10. *Meetings:* General meetings of the Council are convened at least once every two years.

12. *Publications:* The Ligue has concluded an arrangement with the *Annals of the Rheumatic Diseases*, B.M.A. House, Tavistock Square, London, W.C.1, U.K., and this journal serves as the official organ of the Ligue.

13. *Relations with Other International Organizations:* The Ligue Européenne contre le Rhumatisme is a section of the Ligue Internationale contre le Rhumatisme.

14. *Short History:* Congress at Copenhagen and Aarhus in September, 1947.

16. *Comments:* Next European Congress will be held at Barcelona in September, 1951.

## SECOND CONGRESS, 1951

The second Congress of the Ligue Européenne contre le Rhumatisme will be held in Barcelona, Spain, from September 24-27, 1951, when the Sociedad Española de Reumatismo will act as host.

The following subjects will be discussed:

Non-articular Rheumatism.
Effects of Pituitary and Adrenal Cortex Hormones in Rheumatic Disease.
Ultrasonic Therapy.
Ankylosing Spondylitis.
Brucellar Rheumatism.

W. S. C. COPEMAN, *President.*
GUNNAR EDSTRÖM, *Secretary-General.*

London, July 24, 1950.

## LIGUE BELGE CONTRE LE RHUMATISME

A letter received from the Secretary with a copy of a statement issued to the Belgian press is given below (in translation):

*Liège. June* 25, 1950.

To the Editor of the *Annals of the Rheumatic Diseases.*

DEAR SIR,

We beg to enclose for your information a copy of a notice recently published in the Belgian press by the Belgian League against Rheumatism.

Yours faithfully,

M. ORY (*Secretary*).

The Belgian League against Rheumatism, having studied the work of foreign research and the observations of its own members on the action of the combination of desoxycorticosterone and vitamin C upon rheumatoid arthritis, asserts that this combination, as contrasted with cortisone, Compound F, and ACTH (adrenocorticotrophic hormone), has no significant effect upon this disease.

Having regard to the present impossibility of obtaining supplies of cortisone, Compound F, and ACTH, the League warns practitioners against the use of any new steroid the properties of which have not been tested according to the standards of the International League against Rheumatism.

## SOCIETÀ ITALIANA PER LO STUDIO DEL REUMATISMO

The Congress of the Italian Society for the Study of Rheumatism and the Campaign against Rheumatic Diseases, took place at Salsomaggiore on June 19, 1950.

Prof. Giuseppe Sabatini, Director of the Clinical Hospital, University of Genoa, was appointed President by the managing board of the Society.

The next Congress will take place in Naples in conjunction with the Italian Cardiological Society.

## CANADIAN RHEUMATISM ASSOCIATION

### OFFICERS FOR 1950-51

The Executive of the Canadian Rheumatism Association for the period June, 1950 to June, 1951, will be constituted as follows:

| | |
|---|---|
| *Past President:* | Dr. A. W. Bagnall, 832 Medical-Dental Building, Vancouver, B.C., Canada. |
| *President:* | Dr. Henry P. Wright, 4080 Highland Avenue, Montreal, Quebec, Canada. |
| *First Vice-President:* | Dr. W. S. Barnhart, 104 Medical Arts Building, Ottawa, Ontario, Canada. |
| *Second Vice-President:* | Dr. Henry Moyse, Summerside, P.E.I., Canada. |
| *Secretary-Treasurer:* | Dr. Donald C. Graham, Suite 700, Medical Arts Building, Toronto, Ontario, Canada. |

# BOOK REVIEWS

**The Scourge of Rheumatism.** Wm. Heinemann, Medical Books Ltd., London. Pp. 85. 5*s*.

This report of the proceedings at a conference held by the British Rheumatism Association opens with addresses by well known authorities on the treatment and general management of rheumatoid arthritis, which may be read with profit by the laity, since they bring the newest remedies into due perspective and correct erroneous ideas. The problem of the rural patient living often at a distance from any centre for treatment was thoroughly discussed and the need for physiotherapists in the smaller towns and villages emphasized. This is a matter which might well receive consideration as a part of the National Health Service, the available directories of physiotherapists seem to suggest that in many large towns there are far more than can make a living while in the smaller centres there are none. This is probably because the amount of work would be insufficient to provide a reasonable income, and a car might be a necessity and some form of subsidy or salary would be required, some arrangement of the kind would certainly relieve the strain on the ambulance service in many districts and thus effect an economy. The patient who is housebound, either from the degree of crippling or the burden of domestic duties, might find a visiting physiotherapist a great boon.

Rehabilitation, the provision for employment of those who are crippled, and the work of existing voluntary organizations furnish the material for other addresses and discussions, and indicate how wide is the field for the further work which the British Rheumatic Association is seeking to do. This little book deserves to be widely read.

C. W. BUCKLEY.

**The Merck Manual of Diagnosis and Therapy** (1950), 8th ed. Merck and Co. Inc., New Jersey, U.S.A. Pp. 1592. Thumb-index. $5.00.

The sub-title of this book, " A Source of Ready Reference for the Physician ", indicates its object and scope. It is fifty years since the first edition was published and its growth in popularity is demonstrated by the fact that the first printing of 75,000 copies of the eighth edition was exhausted by the date of publication. The manual is edited by a staff of twelve physicians with the assistance as advisers and consultants of a hundred clinicians throughout the United States, and has now been brought right up to date, reflecting the phenomenal advances in medical science in the last decade. It deals for the most part with diagnosis and treatment, but other important aspects of medicine have not been neglected. Every known disease, including many that are extremely rare, appears to be described, and there are valuable chapters on routine immunization procedures, laboratory tests within the scope of the general practitioner, the general management of the patient before and after operation, and much practical advice on clinical and bedside procedures, nursing, diets, etc.

The remedies advised in treatment are an important feature, full prescriptions being given at the end of each section. Surgical operations are indicated where needed but are not described. Homely remedies rarely referred to in the student's training are also included. If any criticism is called for, it might be that the use of physiotherapeutic measures does not receive the attention which might be expected. The chapter on antibiotic therapy deals with the newest discoveries in this field, and the table of chemotherapy suitable for the more common infections is likely to prove very useful.

The essential clinical features of each disease are described fully though briefly. The latest available information on cortisone and ACTH is given, including clinical results

to date in many diseases, and also metabolic, hormonal, and other physiologic effects. The Manual runs to close on 1,600 pages, but is nevertheless within the limits of size and weight which justify its description as a handbook, owing to the thinness of the paper and the general arrangement. It will be found of the greatest assistance to the busy general practitioner to whom it may be strongly recommended. C. W. BUCKLEY.

## HOSPITAL REPORTS

Reports have been received of the work which is being done in some of the hospitals specializing in the treatment of rheumatic diseases, and in research, clinical and laboratory. These furnish most encouraging evidence of the progress which is being made in some centres in the campaign against rheumatism.

**West London Hospital: Department of Rheumatic Diseases.** Annual Report for 1949.

Great progress is being made at this centre, which possesses a large staff of skilled workers including holders of Research Fellowships and Studentships. A peripheral clinic established in 1946 is doing good work, and co-operation has been established with the British Post-graduate Hospital. Twelve beds are available for in-patients at the West London Hospital and the Hospital of St. John and St. Elizabeth, St. John's Wood, and further beds are shortly to be provided at St. Mary Abbots Hospital, Kensington.

A special research department has been established to which the Medical Research Council has made a large grant to aid study of the effects of cortisone in rheumatic disease and generous grants have also been made by the Dan Mason Research Fellowship of the West London Hospital Medical School; in addition Roche Products Limited have, through the Empire Rheumatism Council, presented a Roche Fellowship tenable for two years for a steroid chemist. The Report contains interesting and important papers by members of the staff, notably one by Dr. P. M. F. Bishop on the bio-chemical and endocrine aspects of cortisone, and one by Dr. A. A. Henly on the adrenocorticotrophic hormone. A list of papers from members of the staff, published elsewhere, is also included. A grant from the British Schering Co. Ltd., has rendered possible this very full and well-produced report.

**The Royal Free Hospital: Unit of Rheumatology.** Report for 1949.

Important work is being done at this centre; statistics are given of the numbers treated and the results, and the figures show very encouraging improvement in the results of treatment of ankylosing spondylitis. It is pointed out that the long waiting list militates against efficient treatment in hospital of rheumatoid arthritis, cases lose ground often to a serious degree while waiting for admission and the shortage of beds for chronic cases is also a serious matter. Valuable work is being done by the Almoners and useful statistics have been compiled showing that only a small proportion of the cases which have been under treatment relapse. Special attention is being given to the treatment of certain deformities and to rehabilitation, and research in various directions is being actively carried out.

**Royal National Hospital for Rheumatic Diseases, Bath.** Vol. 3, 1948-49.

Here the formation of a research unit in connection with the South-Western and Oxford Regional Hospital Boards has been an important development; the unit has fifty beds and its own laboratory, and a further seventy beds are available for teaching and research. The staff of the research unit consists of four Research Fellows, and the junior hospital staff has been expanded to include a Senior Registrar, two Registrars, and three House Physicians. Further developments, especially in the Manor Hospital for orthopaedic work, are likely in the near future. The Report also includes reprints of papers contributed by members of the staff to various journals. C.W.B.

# ABSTRACTS

*[This section of the* ANNALS *is published in collaboration with the two abstracting Journals,* Abstracts of World Medicine, *and* Abstracts of World Surgery, Obstetrics and Gynaecology, *published by the British Medical Association. The abstracts are divided into the following sections: acute rheumatism; chronic articular rheumatism (rheumatoid arthritis, osteo-arthritis, spondylitis, miscellaneous); sciatica; gout; non-articular rheumatism; endocrinology; general pathology; other general articles. At the end of each section is a list of titles of articles noted but not abstracted. Not all sections may be represented in any one issue.]*

## Acute Rheumatism

**Oral Penicillin Prophylaxis of Recurrences of Rheumatic Fever. Interim Report on Method After a Three Year Study.** KOHN, K. H., MILZER, A., and MACLEAN, H. (1950). *J. Amer. med. Ass.*, **142**, 20.

A study of the effect of oral penicillin in preventing recurrences of rheumatic fever was carried out on 126 children in a special school in Chicago for cases of rheumatic heart disease. The subjects were divided into two groups, comparable as to sex, race, age, and economic level, one being used as a control. A further control group of eighty children at another similar school were selected in the same manner but were not in contact with those undergoing prophylactic treatment.

Penicillin was given in the hope that it might be possible thus to eliminate haemolytic streptococci and so to prevent or lower the incidence of rheumatic fever. For the former purpose, throat swabs from all the groups of children were examined at intervals during the course of treatment. At the end of 4 months' treatment with 50,000 units of penicillin twice daily, throat swabs showed no improvement in the treated group.

As it was thought that this dosage might be causing penicillin-resistance in the organisms the dosage of penicillin was changed to 1 mega unit daily for 5 days, repeated five times in the school year. This was found to cause a maximum reduction in streptococci in throat swabs from the treated children lasting for at least 3 weeks after the short course.

As a result, in the third year of the experiment, treatment was given in the first week of each calendar month throughout the school year and consisted of 200,000 units four times, or 250,000 units thrice daily for 7 days. With this dosage the penicillin-treated group showed a consistently lower infection rate than did the control group from the same school. Owing probably to the lessened cross-infection risk, the latter group showed a markedly lower infection rate than did the group from the second school, in which the rate was similar, on the one occasion of comparison, to the rate among children in an ordinary school.

The recurrence rate of rheumatic fever in each of the 3 years remained steady at about 20 per cent. in the school where there was no prophylaxis. In the school with prophylaxis the rate among those given penicillin was consistently less than in the control group, though of doubtful significance in the first and second years. In the third year, however, there were no recurrences among the treated children, as compared with 11 per cent. among the untreated. This is regarded as a highly promising result.

During the second and third years, while penicillin was being given in larger doses for short periods, there was no evidence of the development of penicillin resistance among haemolytic streptococci of groups A, B, or C, in a total of 274 strains examined.

*Reginald St. A. Heathcote.*

**Studies of Rheumatic Fever. Comparative Value of the Weltmann Serocoagulation Reaction and the Sedimentation Rate (Cutler) in Determining Activity of the Rheumatic Process.** NELSON, H. G., and SEAL, J. R. (1950). *J. Lab. clin. Med.*, **35**, 220.

An analysis was made of 400 cases of rheumatic fever during convalescence, the patients being men between the ages of 18 and 25 at an American Naval Hospital. Full clinical reports in a standard form were rendered weekly by the ward medical officer, an attempt being made so far as possible to exclude bias from the previous week's laboratory findings. A series of estimations of the Weltmann reaction (coagulation of the patient's serum when incubated with differing concentrations of calcium chloride solution) and the Cutler erythrocyte sedimentation rate (E.S.R.) were made in each case; only those cases with more than four estimations of each were included in this series. A total of 2,552 estimations of each test were performed.

Of the 400 cases fifty showed clinical activity of the rheumatic process during the initial period of convalescence. The results of the Weltmann test showed agreement with the clinical opinion in 60 per cent. of the estimations performed, and the E.S.R. agreed with the clinical findings in 70 per cent. Many of the discrepancies observed were confined to the results of tests on only four patients; when these were allowed for the correlations became 93 per cent. and 90 per cent. respectively. When the disease became clinically inactive in these 46 patients, there was correlation with the Weltmann reaction in 99 per cent. of estimations and the E.S.R. in 93 per cent. Of the 350 cases without clinical activity there was correlation in 98·1 per cent. of Weltmann reactions and in 85·9 per cent. of E.S.R. estimations.

Statistical analysis of these figures proved that a disproportionately large number of those estimations of the E.S.R. showing a discrepancy were confined to a few patients. When 22 patients with four or more abnormal readings of the E.S.R. were excluded, the correlation became 92·2 per cent. No persistent discrepancies with the Weltmann reaction were noted.

The authors conclude that the Weltmann reaction is of great value in the assessment of activity of the rheumatic process, especially when there is no correlation between the E.S.R. and the clinical opinion.

[It is perhaps unfortunate that the authors have used as one of their yardsticks their own modification of the Cutler technique, the test they describe being almost a

Westergren reaction performed in a Cutler tube. Workers using the Wintrobe technique have found a much higher correlation between the clinical activity and the erythrocyte sedimentation rate.]

*A. Michael Davies.*

**The Mode of Action of Salicylate in Acute Rheumatic Fever.** REID, J., WATSON, R. D., and SPROULL, D. H. (1950). *Quart. J. Med.*, **19**, 1.

This paper describes biochemical investigations carried out by the authors on seven adults with rheumatic fever under treatment with salicylate. As a result of these tests they conclude that, although the primary mode of action of salicylate remains uncertain, the principal pharmacological actions of the drug are: (1) induction of respiratory alkalosis, and (2) stimulation of protein catabolism. The details of these actions are as follows:

(1) It is shown by the authors that as the plasma salicylate level rises the plasma carbon-dioxide content falls and the plasma *p*H rises. This correlation shows that carbon dioxide is removed from the plasma by the lungs (probably by the stimulating action of the drug on the vagal nerve-endings causing hyperpnoea) much more rapidly than the fixed base is excreted by the kidneys. Hence the $H_2CO_3$: $NaHCO_3$ ratio diminishes and the plasma *p*H therefore rises. In other words, salicylate appears to induce respiratory alkalosis, clinically manifested by deep breathing.

(2) Protein catabolism profoundly alters the water balance of the body. At first, reduction in intracellular (protoplasmic) water content occurs followed by diminution in extracellular (tissue and plasma) water content, indicated by a fall in plasma volume and the development of a diuresis. It is shown that the former is associated with relief of joint pain and swelling, and the latter with a fall in erythrocyte sedimentation rate.

The authors also observed that salicylate, besides promptly relieving acute manifestations of rheumatic fever, produces a "special salicylate syndrome" with hyperpnoea, sinus bradycardia, peripheral vasodilation, nausea, vomiting, tinnitus, deafness, and drowsiness leading to mental confusion and coma. This syndrome appears when acute manifestations of rheumatic fever are eased and the authors found that the promptness of relief of rheumatic symptoms and the severity of the special salicylate syndrome are both directly related to plasma salicylate level; the higher this level the quicker the disappearance of fever, tachycardia, and joint pain and swelling, and the more intense the symptoms of the added salicylate syndrome. *S. Karani.*

**The Protective Effect of Sodium Salicylate on Serum Induced Myocarditis in Rabbits.** MACGREGOR, A. G., and WOOD, D. R. (1950). *Brit. J. Pharmacol.*, **5**, 9.

Sterile horse serum was injected into 24 young rabbits on the 1st and 20th days, each animal receiving 10 ml. per kg. intravenously on each occasion. Twelve rabbits were given sodium salicylate from the day of the first serum injection. Two daily doses were given orally at 10 a.m. and 4 p.m. and a larger dose was injected subcutaneously at 10 p.m. The final dosage used was 150 mg. per kg. orally and 200 mg. per kg. subcutaneously, a total of 500 mg. per kg. Treatment was continued up to the 26th day, when the surviving animals were killed and their hearts removed for section. In assessing the severity of the lesions produced in each animal (corresponding to those seen in the experimental production of rheumatic fever), marks were awarded for the presence of intermuscular and perivascular infiltration, Aschoff-like bodies, valvular lesions, and muscle and collagen degeneration. The incidence of vascular and valvular lesions was considerably reduced by the treatment with sodium salicylate. The mechanism by which this inhibition is produced is still uncertain.

It may be that the *in vitro* activity of salicylates in inhibiting the activity of hyaluronidase is involved. This enzyme is said to play a part in the breakdown of interfibrillar cement in rheumatic fever. *G. B. West.*

**Cerebral Lesions Responsible for Death of Patients with Active Rheumatic Fever.** COSTERO, I. (1949). *Arch. Neurol. Psychiat., Chicago*, **62**, 48.

**Etiology of Rheumatic Fever.** WAGNER, B. M. (1949). *Arch. Pediat.*, **66**, 301.

**Cardiac Enlargement in Uncomplicated Mitral Insufficiency in Children.** MILLER, J. H., and WEDUM, B. G. (1949). *Amer. J. Dis. Child.*, **78**, 703.

**Penicillin Resistance of Nonhemolytic Streptococci from Rheumatic Children Receiving Prophylactic Penicillin.** KRUMWIEDE, E. (1949). *Pediatrics*, **4**, 634.

**Rheumatic Fever in Adults.** (Rheumás láz a felnóttkorban). CZONICZER, G. (1949). *Orv. Lapja*, **5**, 721.

**Nutrition in Rheumatic Fever.** JACKSON, R. L., and KELLY, H. G. (1949). *J. Amer. diet. Ass.*, **25**, 392.

**Rheumatic Heart Disease in Pregnancy. A Critique of the Rules in Management.** GORENBERG, H. (1949). *Bull. M. Hague Maternt. Hosp.*, **2**, 44.

**Remarks on the Action of Heparin in Acute Rheumatism.** (Remarques sur l'action de l'héparine dans la maladie rhumatismale.) DONZELOT, E., and KAUFMANN, H. (1949). *Méd. français, Paris*, **9**, 179.

**Cardiac Lesions in Rheumatic Fever. Classification.** (Lesiones cardíacas de la fiebre ruemática. Definición de formas y clasificación.) RAMOS, F. H., and CORREA, B. D. (1948). *Bol. Liga urug. Reum.*, **2**, 159.

**A Study of the Q-T Interval in Rheumatic Fever.** POKRESS, M. J., and GOLDBERGER, E. (1949). *Amer. Heart J.*, **38**, 423.

**Cerebral Edema Complicating Active Rheumatic Heart Disease in a Child.** KOWALOFF, I. (1949). *N.Y. St. J. Med.*, **49**, 2183.

**A Clinical and Statistical Study of the Course and Prognosis of Rheumatic Heart Disease. III. Rheumatic Valvular Defects in Persons Over 45.** (Studio clinico-statistico sulla evoluzione e prognosi della cardiopatia reumatica. III-I vizi cardiaci di origine reumatica nei soggetti di eta' superiore a 45 anni.) MASINI, V. (1949). *Cuore e Circol.*, **33**, 76.

**Convalescent Care of Rheumatic Fever in the Home.** DENNISON, A. D. (1949). *J. med. Soc. N.J.*, **46**, 437.

**The Effect of Artificial Pyrexia on the Clinical Picture of Acute Rheumatic and Allergic Conditions and its Significance for the Theoretical Study of Acute Rheumatism.** (Über die Wirkung der Fieberschockbehandlung Akuter Rheumatischer und Allergischer Krankheitsbilder und ihre Bedeutung für die Theorie des Akuten Rheumatismus.) SCHMENGLER, F.-E. (1949). *Klin. Wschr.*, **27**, 627.

**Rheumatic Fever and Rheumatic Heart Disease in Children. Diagnosis and Treatment.** TARAN, L. M. (1949). *J. Mich. med. Soc.*, **48**, 1121.

**Group A Streptococcal Infections and Rheumatic Fever.** ROTHBARD, S. (1949). *J. Mich. med. Soc.*, **48**, 1126.

**The Physician and Community Action for Rheumatic Fever.** WHEATLEY, G. M. (1949). *J. Mich. med. Soc.*, **48**, 1128.

**Rheumatic Angina Pectoris.** (L'Angine de poitrine rhumatismale.) LÉVY, G. (1949). *Pr. méd.*, **57**, 887.

**Intravenous Sodium Salicylate in the Treatment of Two Cases of Acute Articular Rheumatism with Spectacular Effect on the Course of the Disease.** (Deux cas de rhumatisme articulaire aigu, traités par perfusion intraveineuse de salicylate de soude. Action spectaculaire du choc médicamenteux sur le cours de la maladie.) BOQUIEN, Y., HERVOUET, D., DAUPHIN, —., and ERIMBERGER, —. (1949). *Bull. Soc. méd. Hôp. Paris*, **65**, 1232.

**Modern Treatment of Acute Articular Rheumatism.** (Moderno trattamento del reumatismo articolare acuto.) CORELLI, F. (1949). *Minerva med., Torino*, **40**, 516.

**Aetiology, Prophylaxis and Treatment of Rheumatic Fever.** (Etiologia, profilaxis y tratamiento de la fiebre reumática.) MALDONADO-ALLENDE, I. (1949). *Prensa méd. argent.*, **36**, 1885.

**The Anti-exudative Action of Heparin in Acute Rheumatism.** (Héparine et rhumatisme. L'action anti-exsudative de l'héparine.) DONZELOT, E., and KAUFMANN, H. (1949). *Pr. méd.*, **57**, 989.

**A Study of Rheumatic Heart Disease in Bombay Province.** VAKIL, R. J. (1949). *Indian Heart J.*, **1**, 15.

**Some Observations on the Past History and Clinical Findings in Rheumatic Heart Disease as Found in Bengal.** BOSE, A. K. (1949). *Indian Heart J.*, **1**, 68.

**Clinical Observation on so-called Scarlatinal Rheumatism.** (Osservazioni cliniche sul cosidetto reumatismo scarlattinoso.) AGNOLI, R. (1949). *Inform. med., Genova*, **3**, 3.

**Modern Treatment of Acute Rheumatism in Childhood.** BABER, M. D. (1949). *Med. Pr.*, **111**, 93.

**The Etiology of Rheumatic Fever : A Review of Theories and Evidence.** WAKSMAN, B. H. (1949). *Medicine, Baltimore*, **28**, 143.

**Prolonged Rest v. Ambulatory Treatment of Rheumatic Fever.** KURTZ, C. M. (1949). *Wis. med. J.*, **48**, 498.

**The Management of Rheumatic Heart Disease.** ANGLIN, A. (1949). *N.S. med. Bull.*, **28**, 113.

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**The Syndrome of Acute Articular Rheumatism.** (Le syndrome rhumatisme articulaire aigu.) ROUVEIX, J. (1949). *Concours Méd.*, **71**, 1271.

**Meningeal Reaction in Rheumatic Fever.** (Sulla reattività meningea nella malattia reumatica.) NASSI, L. (1950). *Riv. Clin. pediat.*, **47**, 529.

**Rheumatic Fever.** SHIRLEY, R. G. (1950). *Calif. Med.*, **72**, 85.

**Prevalence of Rheumatic Heart Disease at High Altitudes.** WEDUM, B. G., DARLEY, W., and RHODES, P. H. (1950). *Amer. J. Dis. Child.*, **79**, 205.

**The Treatment of Rheumatic Fever with Pancarditis in Salicylate-refractory Cases.** (Zur Therapie salicylrefraktärer Polyarthritis rheumatica mit Pancarditis.) JAHNKE, K. H. (1950). *Med. Klinik.*, **45**, 78.

**Rheumatic Fever.** HOBBS, T. G. (1950). *Kentucky med. J.*, **48**, 57.

**Rheumatic Fever Statistics in Denmark from 1878 to 1946 and their Significance in Prophylaxis.** CLEMMESEN, S. (1949). *Acta med. scand., Suppl.*, **136**, 109.

**Mester's Test in the Diagnosis of Acute Rheumatism.** (La Prova di mester nella diagnosi della malattia reumatica.) PASSARO, G. (1950). *Arch. ital. Pediat.*, **13**, 384.

**Eosinophilia in Acute Rheumatic Fever.** KREBS, G. C., and STEVENSON, C. P. (1950). *Rocky Mtn med. J.*, **47**, 278.

**Respiratory Manifestation of Acute Rheumatism.** (Le manifestazioni respiratorie del reumatismo articolare acuto.) CHIERICHETTI, M. (1950). *Ann. ital. Pediat.*, **3**, 164.

**An Investigation of Rheumatic Fever in Fiji.** BARNES, G. (1950). *Trans. R. Soc. trop. Med. Hyg.*, **43**, 413.

**Deaths from Acute Rheumatic Fever in Texas : Relationship to Mean January Temperature.** HEYER, H. E., HANSEN, A. E., CHAPMAN, D. W., ADAMSON, W. B., and PARSONS, G. W. (1950). *Amer. J. med. Sci.*, **219**, 40.

**Treatment of Rheumatic Fever. Extensive Experience and a Personal Hypothesis.** (El tratamiento de la fiebre reumatica. Una larga experiencia y una hipotesis personal.) PASQUALINI, R. Q. (1950). *Prensa méd. argent.*, **37**, 757.

**Cardiac Changes in Rheumatic Arthritis.** (Herzveränderungen beim primär chronischen Gelenkrheumatismus.) SCHNELLER, —. (1950). *Med. Klinik.*, **45**, 271.

**Rheumatic Fever with Nodules in a Child of 7 months.** (Rheumatismus nodosus im 7. Lebensmonat.) THALHAMMER, O. (1950). *Ost. Z. Kinderheilk.*, **4**, 201.

## Chronic Articular Rheumatism (Rheumatoid Arthritis)

**Dysphagia in Felty's Syndrome.** [In English.] LINDEBOOM, G. A. (1949-50). *Gastroenterologia, Basel*, **75**, 129.

The Plummer-Vinson syndrome, usually seen in middle-aged women, is characterized by hypochromic anaemia and dysphagia; occasionally, the changes in the oral epithelium suggest a deficiency of the vitamin-B complex, though administration of the latter alone does not cure the condition. The relation between it and Sjögren's disease (dacryo-sialo-adenopathia atrophicans) has been discussed by Godtfredsen, who observed 23 cases of the disease and found that in thirteen there was dysphagia and in three the complete Plummer-Vinson syndrome; most of his patients had a chronic progressive polyarthritis. Felty's syndrome is characterized by rheumatoid arthritis, splenomegaly, and leucopenia, and may be associated with a pronounced dysphagia. Anaemia is a common factor in all three conditions.

The author describes Felty's syndrome in one male and one female patient; both had severe dysphagia and the woman had advanced cancer of the uterine cervix. He discusses the advisability of splenectomy and quotes the conflicting views of various authorities. He hints that patients with Felty's syndrome do not form a homogeneous group and suggests that the presence of cancer in the second case described was not coincidental. In support of this view he mentions a paper by Ayre (*Amer. J. Obstet. Gynec.*, 1947, **54**, 363) who sought to establish a connexion between cervical cancer and nutritional deficiency. *D. Preiskel.*

**Copper Morrhuate in Treatment of Rheumatoid Arthritis.** (Le morrhuate de cuivre dans la thérapeutique des polyartites chroniques.) GRABER-DUVERNAY, J., and VAN MOORLEGHEM, G. (1950). *Lyon méd.*, **183**, 113.

The authors describe preliminary results with copper morrhuate in the treatment of rheumatoid arthritis.

Their studies started in 1943 when they gave intravenous injections of cod-liver oil to seven patients. In two of these patients a striking therapeutic result was obtained, bedridden patients being able to resume full activity after six injections. Reactions were, however, so severe in two cases that the method was abandoned.

The next stage was the employment of ethyl morrhuate in a series of cases by intramuscular injection. In four cases out of seven pain was relieved, physical signs diminished, the patient gained weight, and the erythrocyte sedimentation rate fell after a course of twenty injections of 50 mg. every other day. Tolerance was perfect.

The authors have now prepared a colloidal solution of copper morrhuate which remains stable indefinitely. Each ampoule contains 50 mg. morrhuate and either 2 or 10 mg. copper. The preparation may be given intravenously, in which case injection should be very slow, or intramuscularly, in which case procaine must be added. A course consists of 24 to 32 injections, at first of 2 mg. copper, then of 10 mg. two or three times a week. The effect of this preparation is greater than that of ethyl morrhuate. No serious reaction has been observed. In a series of 117 cases improvement has been obtained in about 30 to 35 per cent. This low figure is attributable to the fact that cases have not been selected. *S. S. B. Gilder.*

**Effects of Delta 5 Pregnenolone in Rheumatoid Arthritis.** DAVIDSON, R., KOETS, P., SNOW, W. G., and GABRIELSON, L. G. (1950). *Arch. intern. Med.*, **85**, 365.

The authors claim, in this further paper on the relation of steroid metabolism to rheumatoid arthritis, that the synthetic steroid $\Delta^5$-pregnenolone, when administered in adequate dosage by intramuscular injection, will cause a remission in the course of rheumatoid arthritis, and that this remission can be maintained by means of a suitable scale of dosage. When the injections are stopped the activity of the disease will return within a few days. No toxic effects of any sort have been observed in patients given daily injections for periods up to 4 months.

It is claimed that although pregnenolone takes much longer to become effective than do cortisone or pituitary adrenocorticotrophic hormone, its lack of toxicity and low cost of manufacture are determining factors in favour of its use. High dosage is essential, the average effective daily dose being in the neighbourhood of 200 mg. Once symptomatic improvement has become manifest, 100 mg. daily will generally prove sufficient to maintain it. It is stated that a new substance which permits of the employment of still larger dosage without toxicity symptoms is at present under test. Full reports on thirteen cases are appended.

[The confusion of ankylosing spondylitis with rheumatoid arthritis (" rheumatoid spondylitis ") which is so usual in American papers, somewhat vitiates the value of this paper. In spite of the title, it seems that it is principally for the treatment of ankylosing spondylitis that the authors recommend the use of this steroid, although they report favourable results in both conditions.] *W. S. C. Copeman.*

**Diagnostic Value of Histologic Lesions of Striated Muscle in Rheumatoid Arthritis.** SOLOKOFF, L., WILENS, S. L., BUNIM, J. J., and MCEWEN, C. (1950). *Amer. J. med. Sci.*, **219**, 174.

Biopsy or necropsy specimens of muscle from the deltoid and gastrocnemius were examined by serial section in 57 cases of rheumatoid arthritis, ten of ankylosing spondylitis, 21 of acute rheumatism, 101 of various other conditions, some involving the joints, and in thirteen healthy volunteers. Focal cellular lesions similar to those described by other workers were found in 56 per cent. of the cases of rheumatoid arthritis, but also in three of the normal controls and in 25 per cent. of the non-rheumatoid group as a whole. Various other laboratory investigations were performed, such as determination of the erythrocyte sedimentation rate and estimation of the serum content of streptococcal

agglutinins and agglutinin of sensitized sheep erythrocytes. None of these threw any light on the mechanism of production of the histological lesions, and the authors conclude that muscle biopsy is of little value as a diagnostic procedure in rheumatoid arthritis.

*G. J. Cunningham.*

**A Principle for Determining Prognosis of Pregnancy in Rheumatic Heart Disease.** BUNIM, J. J., and APPEL, S. B. (1950). *J. Amer. med. Ass.*, **142**, 90.

**Cuprotherapy in Rheumatoid Arthritis.** (La cuprotherapie en cas de polyarthrite primaire chronique.) BLÉCOURT, J. J. (1950). *Rev. Rhum.*, **17**, 16.

**Function of the Liver During Sanocrysin Treatment of Rheumatoid Arthritis. Estimated by Means of the Thymol Reaction.** POULSEN, E. (1949). *Acta med. scand., Suppl.*, **136**, 268.

**Therapeutic Value of Copper Salts in Rheumatoid Arthritis.** FORESTIER, J., CERTONCINY, A., and JACQUELINE, F. (1950). *Stanford med. Bull.*, **8**, 12.

**Chrysotherapy in Rheumatoid Arthritis.** NEUDORFF, L. G. (1950). *J. Mo. med. Ass.*, **47**, 172.

**Intravascular Aggregation of the Erythrocytes in Rheumatoid Arthritis.** LAINE, V., and ZILLIACUS, H. (1950). *Acta med. scand.*, **137**, 87.

**Modern Concepts in the Appreciation of Rheumatoid Arthritis.** PATTERSON, J. W. T. (1950). *Bgham med. Rev.*, **16**, 219.

**The Pathological Anatomy of Rheumatoid Arthritis.** (Réflexions sur l'anatomie pathologique des polyarthrites chroniques évolutives.) RAVAULT, P., and VIGNON, G. (1949). *Rhumatologie*, **1**, 278.

**Prevention and Treatment of Deformities in Rheumatoid Arthritis.** HILL, D. F., and HOLBROOK, W. P. (1950). *J. Amer. med. Ass.*, **142**, 718.

**Hypercalcaemia During Vitamin-D Treatment of Rheumatoid Arthritis.** ADDIS, H. St. C. C., and CURRIE, R. D. (1950). *Brit. med. J.*, **1**, 877.

## (Osteo-Arthritis)

**Temporomandibular Arthrosis.** FOGED, J. (1949). *Lancet*, **2**, 1209.

The author suggested in 1940 that the condition causing "cracking" of the jaw should be called "temporomandibular arthrosis" as he considers that it is a degenerative, non-infective disease of the joint and that the characteristic snapping " is merely one of several symptoms in the more serious cases ". He has studied 138 examples in the last 9 years and finds it commonest between 20 and 30 years old (though the total age distribution is wide), the sex-ratio being 4½ female cases to one male case. He considers that there are many predisposing causes, but emphasizes the importance of dental irregularities with resulting repeated trauma from an abnormal bite. This produces pain and stiffness which is later followed by restrictive movement of the joint which may even interfere with nutrition. Deviation of the chin to the affected side on opening the mouth was a conspicuous sign in over one-half of the unilateral examples. *X*-ray examination, with or without arthrography, often showed changes in the joint, but the erythrocyte sedimentation rate was normal and other pathological tests gave negative results.

Emphasis is laid on the need for an expert dental opinion in deciding the cause and suggesting conservative methods of treatment, which are often successful, but are protracted and expensive in Denmark. The indications for operation, which was carried out in about 1 in 4 of the author's cases, are listed, the most important being progressive limitation of movement and frequent locking. Some form of local analgesia is preferred by the author who uses the posterior approach (Bockenheimer-Axhausen) to divide adhesions and usually to excise the meniscus, with occasional removal of the condyle. Good results are claimed in 32 of 41 cases (33 patients) after a follow-up of 6 months to 8 years, and there were no complications, apart from partial and transient facial paralysis, in ten cases. *Eric I. Lloyd.*

**Vitallium-cup Arthroplasty of the Hip Joint. Review of Approximately One Hundred Cases.** GIBSON, A. (1949). *J. Bone Jt Surg.*, **31A**, 861.

The author suggests that muscular insufficiency is an important factor in the development of osteo-arthritis of the hip, and that the deformities in the femoral head and acetabulum are the result of misdirected physical strain. He presents his impressions (rather than a statistical analysis) of the results in 111 cases treated by vitallium-mould arthroplasty. The best results were obtained in osteoarthritis (89 cases). In atrophic arthritis nine cases) and Marie-Strümpell disease (three) the operation proved disappointing, whereas no success was achieved in tuberculous arthritis (two). In cases of un-united fracture of the neck of the femur (three), old slipped upper femoral epiphysis (two), and septic arthritis (two) unsatisfactory results were obtained, whereas a good result was obtained in one case of fracture dislocation.

The posterior (Kocher) approach to the hip joint was used in every case, and on no occasion was a blood transfusion necessary. The femoral head alone is remodelled, only loose pieces of bone or redundant synovial membrane being removed from the acetabulum. Post-operative treatment consists of 4 weeks in bed, during which time assisted, active, and resisted hip exercises are carried out in all directions, together with exercises for the lumbar spine. Complications in the author's series included infection (one), dislocation (three) transient foot-drop (one), and spur formation on the femoral neck (one). Bone absorption in the acetabulum is noted frequently, and on account of this the author does not advise burring out the cavity of the acetabulum. There were no operative deaths.

Good results, with freedom from pain and adequate function as regards return to work and activity, were obtained in 65 out of 111 cases. A satisfactory result, with the emphasis on alleviation of pain, was obtained in a further sixteen cases, and doubtful or poor results were obtained in thirty cases, which included all the cases of tuberculous, atrophic, and Marie-Strümpell arthritis.

[In the discussion following the presentation of this paper, Smith-Petersen pointed out that this method differs from his own, in which the necessity of the accurate re-shaping of both sides of the joint is stressed, together with the freedom of movement of the vitallium mould in the acetabulum and on the femoral head. He also pointed out that the posterior approach would be less satisfactory in cases of osteo-arthritis when the anterior acetabular bone is hypertrophied, which is frequently the case.]

[This paper would be of much more value if based on a scientific study of results, though the practical difficulties of carrying this out in the area of Winnipeg, Manitoba, where the author works must be fully realized.] *W. A. Law.*

**Procaine Injection for Relief of Pain in the Hip.** ERGENBRIGHT, W. V., and LOWRY, F. C. (1949). *J. Bone Jt Surg.*, **31A**, 820.

A technique is described for the relief of pain from chronic arthritis of the hip, in which procaine is injected into the obturator nerve from in front as it leaves the obturator foramen, and into the nerve to the quadratus from behind where it lies on the posterior surface of the ischium. Nineteen patients out of 23 treated by this method had immediate and complete relief of pain, and eighteen had increased movement. The relief of pain lasted for periods ranging from 36 hours to 3 months.

[The authors' conclusion that, in addition to being a useful means of treatment for coxalgia, this method should be used as a therapeutic test before surgical denervation of the hip, deserves careful consideration by orthopaedic surgeons.] *L. W. Plewes.*

**Early Effects of Partial Sensory Denervation of the Hip for Relief of Pain in Chronic Arthritis.** OBLETZ, B. E., LOCKIE, L. M., MILCH, E., and HYMAN, I. (1949). *J. Bone Jt Surg.*, **31A**, 805.

In this paper the technique and results of operations for partial denervation of the hip joint for the relief of pain in cases of chronic arthritis are discussed. The authors describe four definite patterns of pain arising from disease of the hip joint: (1) Obturator (medial aspect of thigh); (2) Posterior (buttock); (3) Femoral (anterior thigh); (4) Lateral (lateral aspect of thigh). Only patients with the obturator and posterior patterns of pain are considered suitable for operation. Obturator neurectomy may be performed by intrapelvic or extrapelvic approach, but in the authors' experience the latter approach gives much less satisfactory results. Both operations are illustrated and described in detail. Posterior denervation may be performed at the same operation.

Partial denervation was performed in 48 cases where conservative therapy had failed and major operative procedures were contraindicated. During an observation period after operation ranging from 3 to 20 months, 66 per cent. of the patients were appreciably relieved of pain. Most of the failures occurred in those cases where the extrapelvic approach was used for obturator neurectomy. Electromyographic tracings are reproduced showing the marked effect of intrapelvic section of one obturator nerve on adductor spasm in a case of bilateral osteo-arthritis of the hip, the tracing from the untreated side remaining as a control. *L. W. Plewes.*

**Osteoarthritis of the Trapeziometacarpal Joint.** LASSERRE, C., PAUZAT, P., and DERENNES, R. (1949). *J. Bone Jt Surg.*, **31B**, 534.

The best position for obtaining a radiographic view of the metacarpo-carpal joint of the thumb is described in detail, the importance of placing the hand in full pronation being stressed. Several illustrations of the results of this technique are given. A light plastic splint is recommended for immobilization of the joint when the latter is the site of osteo-arthritis. *John Charnley.*

**Excision of the Trapezium for Osteo-arthritis of the Trapezio-metacarpal Joint.** GERVIS, W. H. (1949). *J. Bone Jt Surg.*, **31B**, 537.

Excision of the trapezium is recommended for osteo-arthritis of the carpo-metacarpal joint of the thumb. The operation has been performed eighteen times, and indifferent results were encountered in only two cases. Both the poor results were in cases with generalized arthritic changes. The results in the remaining sixteen cases were uniformly encouraging. Details of the technique are described. *John Charnley.*

**Rhizotomy in Painful Conditions of the Hip-Joints. A Post-operative Follow-up Study.** [In English.] HERLIN, L. (1949). *Acta chir. scand.*, **99**, 113.

Rhizotomy was performed in 44 cases of painful conditions of the hip-joint during 1943-46. A follow-up questionary after 2 to 5 years gave the following results: of 22 males, nine had satisfactory improvement, four had some improvement, and nine had none; of 22 females, four had satisfactory improvement, five had some improvement,and thirteen had none. Different roots were cut for the relief of pain. The author sees no reason for section of more than the sensory root of L 4, but he suggests that excision of the posterior root ganglion might give better results. *J. Agerholm-Christensen.*

**Articular Statics and Arthritis of the Hip.** (Statique articulaire et coxarthrie.) GRABER-DUVERNAY, J. (1950). *J. Méd. Lyon*, **31**, 301.

## (Spondylitis)

**Treatment of Chronic Spondylarthritis by Parathyroidectomy.** (Príspevok k liečeniu chronických spondylarthritīd parathyroidectomiou.) ČERVEŇANSKY, J., and HORNICKY, P. (1950). *Rozhl. Chir.*, **29**, 1.

Basing their treatment on the work of Oppel of Leningrad, the authors performed parathyroidectomy in four out of five cases of ankylosing spondylarthritis, and thyroidectomy with ligation and resection of the thyroid artery in the other case (in this case the parathyroids could not be located). In four cases the calcium level in blood was normal, and in one case there was hypercalcaemia (17·5 mg. per 100 ml.); this case was the only one in which an adenoma of the parathyroid was found and in which there was a post-operative fall in the blood calcium level greater than the usual 1 to 3 mg. per 100 ml. In all cases there was a remarkable improvement in subjective symptoms immediately after operation, but except in one case this improvement was temporary and lasted only for a few months or years. The rationale of this procedure is not clear, and the

authors incline towards the hypothesis that the upset of endocrine balance caused by parathyroidectomy results in stimulation of the adrenal cortex. *A. Rohan.*

**The Treatment of Ankylosing Spondylitis.** (Le traitement de la Spondylarthrite ankylosante.) GIRARD, M., and ROZIER, M. (1950). *J. Méd. Lyon*, **31**, 305.

**Spondylitis Ankylopoietica: analysis of 23 Cases.** (Espondiloartritis Anquilosante: revision de 23 casos.) LOSADA, M., and FRANCE, O. (1949). *Rev. méd. Chile*, **77**, 760.

**Spondylitis Deformans with the Syndrome of Meralgia Paraesthetica.** (Spondilosi deformante con sindrome di meralgia parestesica.) OLIVIERI, F. (1950). *Policlinico sez. prat.*, **57**, 454.

## (Miscellaneous)

**Hydatid Disease of Vertebrae.** WOODLAND, L. J. (1949). *Med. J. Aust.*, **2**, 904.

Bone involvement by hydatid disease occurs in 2·1 per cent. of all cases. The bones affected are the vertebrae, pelvis, femur, and humerus. The vertebrae are affected in 33 per cent. of cases of bony involvement. Infection occurs in childhood, but hydatid growth is so slow that symptoms do not appear before adult life. The onset is usually shown by either dislocation or collapse of a vertebra or by signs of pressure on the cord. Five cases are reported, in four of which there were signs of cord pressure. Growth is slow at first, but becomes rapid once the hydatids have escaped from the bone. The cysts in bone are as a rule small, but one case in which there was a large cyst is reported. They may begin anywhere in the cancellous tissue of the vertebral body, pedicles, or laminae. Extra-osseous lesions are prone to degenerative change.

The diagnosis is difficult. Radiological signs, though not conclusive, are as a rule more advanced than the duration of symptoms would suggest. The trabecular pattern is destroyed, but the " bunch of grapes " appearance found typically in the ilium is not seen. The intervertebral disk is not involved. There is no periosteal reaction except when secondary infection has occurred. Massive sequestration is rare, but small sequestrae may be present.

In differential diagnosis the following conditions must be considered. (1) Pyogenic osteomyelitis. In both diseases involvement of adjacent vertebrae is common, but in osteomyelitis there is fever, loss of the intervertebral disk, and marked periosteal reaction. (2) Tuberculous spondylitis. The cold abscess may resemble the extra-osseous extension of hydatid disease, but the site of infection, the rarefaction, and loss of the disk spaces are distinctive. (3) Secondary carcinoma. Periosteal reaction is absent, but complete destruction of a single vertebra is the rule. (4) Haemangioma produces a honeycomb rarefaction, without periosteal reaction, confined to one body. (5) Bone sarcoma occurs in the young, though the extra-osseous extensions may suggest those of hydatid disease. Secondaries elsewhere make the diagnosis clear. (6) Syphilitic spondylitis affects chiefly the cervical spine; there is a combination of bone destruction and new bone formation, with the development of spurs. Similar changes are seen in Charcot's disease of the spine. The " bunch of grapes " appearance, if present, may simulate fibrocystic disease or multiple myeloma. Large cysts must be differentiated from simple bone cysts, chondroma, and osteoclastoma.

The disease is very chronic. The time of survival of the four patients who died was 5, 19, 7, and 12 years. The only surviving patient is paraplegic but has lived for nine years. Most patients had undergone numerous laminectomies, with very variable results owing to the inevitable recurrence of pressure on the cord even if this could be temporarily relieved. *J. G. Bonnin.*

**Fluorosis with Report of an Advanced Case.** KILBORN, L. G., OUTERBRIDGE, T. S., and HAI-PENG LEI. (1950) *Canad. med. Ass. J.*, **62**, 135.

An anthropological survey of Miao peasants living in Shih Men K'an in Kweichow Province of Southwest China revealed a very high incidence of " arthritis " and joint ankylosis amongst the adult population of neighbouring villages. These changes proved typical of fluorosis and analysis of the water supplies showed concentrations of fluorine up to 6·28 parts per million. The villagers stated that the disease started at about 10 years of age and in acute cases caused death at about 18. In chronic cases, however, the patient often lived, severely crippled, to the age of 50. The skeleton of one patient who died of a fractured cervical spine—from a trivial fall—was obtained and studied. All the bones were thickened, porous, and brittle. The intervertebral disks were ossified and the whole vertebral column was fused into one long bone. Analysis of the bones revealed a fluorine content nearly twenty times that of normal bones used as controls. *C. Bruce Perry.*

**The Clinical Diagnosis of Periarteritis Nodosa: Report of Four Cases.** KING, B. G. (1950). *Ann. intern. Med.*, **32**, 466.

Because periarteritis nodosa may affect more than one organ or system of the body, the disease gives rise to bizarre and diverse clinical manifestations. It is true that the symptomatology includes fever, asthenia, and loss of weight, but these symptoms are common to many diseases. The diagnosis of periarteritis nodosa should be considered, however, when additional symptoms are produced by vascular abnormalities. Furthermore, the diagnosis should be borne in mind in cases of subacute or chronic conditions of obscure aetiology and when patients are suffering from two apparently unrelated conditions, such as neuritis and nephritis. Biopsy examination of muscles, nodules, and abdominal organs may prove to be of the utmost value.

In a man, aged 36 years, biopsy examination of the left gastrocnemius muscle revealed the lesions of the disease. Significance was attached to the presence of fever, hypertension, haematuria, and muscle pain. Variable changes were detected in the reflexes, and subcutaneous nodules were found in the limbs.

Necropsy findings confirmed the diagnosis in three male patients whose ages ranged from 22 to 34 years. The first patient had fever, hypertension, haematuria, uraemia, and subcutaneous nodules. The heart was found to be

enlarged, and there was evidence of pericarditis. Anaesthesia and pareses developed in the upper limbs. Haematemesis was a terminal event. Widespread lesions were observed at necropsy. Evidently the haematemesis had been due to periarteritis nodosa, for the disease had affected the arteries in a large gastric ulcer. Vascular lesions in the brachial plexus were responsible for the neurological signs. In the second patient the presence of the disease was suspected because the chief manifestations were fever and hypertension combined with changes in the renal tract and nervous system. The third patient required a laparotomy for a perforated peptic ulcer. In other respects his symptoms were somewhat similar to those experienced by the other patients, yet his medical attendants made no fewer than seventeen different diagnoses of the illness. *A. Garland.*

**Arthralgia and Arthritis Caused by Infectious Hepatitis.** [In English.] KLEMOLA, E., and TÖRMÄ, S. (1949). *Ann. Med. intern. fenn.*, **38**, 161.

The authors regard " arthralgia " as a lesion of a joint associated clinically with local pain, stiffness, and tenderness on pressure. On the other hand, when swelling of the joint is present, the patient is said to have an " arthritis ". However, " it was often difficult for the patient to distinguish the muscle pain from the joint pain ". On the basis of such a group of clinical premises an investigation was carried out on the joint manifestations of 150 patients (93 female and 57 male; 82 less and 68 more than 30 years of age) who suffered from infective hepatitis. Jaundice developed in all cases. The joint manifestations were present in the pre-icteric stage in eighteen patients, in the pre-icteric and icteric stages in nineteen, and in the icteric in nine only. Often " arthritis " or " arthralgia " was the presenting feature of the disease and it lasted for periods varying from a week to 3½ months.

The authors go so far as to suggest that the presence of " arthralgia " or " arthritis " may be of value in the differential diagnosis of jaundice. *I. H. Milner.*

**The Mucinoses. A Classification with Histo-chemical Studies on the Nature of Mucin.** PALITZ, L. L., and BRUNNER, M. J. (1950). *J. invest. Derm.*, **14**, 159.

The mucinoses are characterized by the accumulation of mucin in the cutis. They may be classified in two main groups: the myxoedemas or metabolic mucinoses, and the secondary or catabolic mucinoses.

Of the metabolic mucinoses the most common is generalized myxoedema associated with hypothyroidism. The localized myxoedemas may be papular, lichenoid, or nodular, occurring on any part of the body and associated with hypothyroidism. They may occur with past or present thyrotoxicosis as bilateral, irregular, firm plaques, often, but not necessarily, on the pre-tibial area (myxoedema circumscriptum thyrotoxicum), or they may rarely be present as widespread papules with no signs of thyroid dysfunction. Localized myxoedema with hypothyroidism responds to thyroid medication. The pre-tibial type is related to pituitary hormone activity.

Secondary or catabolic mucinoses are a group in which excess mucin is probably formed as a degeneration product of connective tissue. They are found in sarcomata, fibromata, and lipomata.

It is possible that a considerable part of the mucin in myxoedema circumscriptum thyrotoxicum is the mucopolysaccharide hyaluronic acid. In two patients with this condition hyaluronidase (150 turbidity reducing units per ml.) was injected into the pre-tibial lesions daily for 10 days. The lesions became softer and flatter and several months later areas of soft normal skin were found within the area of injection. *S. T. Anning.*

**Evaluation of Histamine and Cholinesterase in Allergic Phenomena.** HJORT, A. M., WORDEN, A. S., and HOGLE, J. (1950). *Ann. intern. Med.*, **32**, 217.

An investigation was carried out to determine the importance of changes in the cholinesterase and histamine content of the blood in allergic states. The cholinesterase activity of cells and serum was estimated by the methods of Alles and Hawes in the blood of a series of allergic subjects. The values were found to fall mainly within normal limits and there was no relation between variations in the level of cholinesterase activity and in those of other constituents of the blood, including serum protein, serum chloride, erythrocytes, or haemoglobin. These results confirm those of other workers.

The blood content of histamine in allergic subjects was estimated by means of dialysis through viscose tubing and by the Code method. The addition of histidine to fresh whole blood, with and without incubation for 15 minutes at 37° C., led to no increase in histamine content. Blood histamine values were found to be consistently lower during the summer months. The incubation of blood with the allergen to which the patient was sensitive led to no significant increase in histamine content. These findings are at variance with those of Katz and Cohen (*J. Amer. med. Ass.*, 1941, **117**, 1782). The authors consider that the finding of normal cholinesterase activity in the blood does not affect the possible significance of the cholinergic nervous system in allergic states, in which there may be hypersensitivity to acetylcholine. They suggest that further work is needed to determine whether histamine is elaborated in the blood of allergic individuals. *R. S. Bruce Pearson.*

**The Effect of Sodium Salicylate Upon Hypersensitivity Reactions.** SMITH, W., and HUMPHREY, J. H. (1949). *Brit. J. exp. Path.*, **30**, 560.

Sodium salicylate in blood concentrations of the order of 50 mg. per 100 ml. confers no appreciable protection against acute anaphylactic shock in guinea-pigs. With the same technique of shock production the antihistamine drug, " antistin ", was found to protect completely against the immediate fatal effects. In passive Arthus reactions in both guinea-pigs and rabbits, sodium salicylate exerts a protective action whilst the anti-histamine drugs are relatively impotent. The same is true to an even greater extent in the case of the Shwartzman phenomenon. This protective effect of sodium salicylate is not a direct anti-histamine effect but appears to be due to some action on the local blood capillaries. The increased capillary permeability which normally occurs in such hypersensitivity reactions is thus prevented. The implications of these results in respect of rheumatic fever are briefly discussed.—[*Authors' summary.*]

**Hyaluronidase Action on the Permeability of Human Skin. Some Experiments, Mainly on Allergic Skin Reactions.** [In English.] ASBOE-HANSEN, G. (1950). *Acta derm.-venereol., Stockh.*, **30**, 27.

The effect of the Duran-Reynals spreading factor or hyaluronidase on healthy human skin was investigated. Extract of bovine testes (2·5 turbidity reducing units per ml. of physiological saline) was used, 0·1 ml. being injected intracutaneously. The spreading effect was estimated from the profile of the wheal produced, by the use of dyes and by means of radioactive substances. The effect of hyaluronidase used in this manner was noted on allergic subjects with allergens injected intracutaneously or applied to a scratch at the site of previous hyaluronidase injection. The wheal resulting from injection of an allergen at such a site disappeared more rapidly than the control wheal; no wheal resulted in such a scratch test though present in the control scratch. With positive patch tests there was no spread of the eczematous reaction in skin treated with hyaluronidase.

Mantoux and trichophytin reactions in skin similarly treated showed less intense inflammation and considerable spreading.

The viscosity of the ground substance of the skin (hyaluronic acid), which is reduced by hyaluronidase, is said to be restored after 48 hours. *S. T. Anning.*

**Fibrous Dysplasia of Bone.** PROFFITT, J. N., MCSWAIN, B., and KALMON, E. H. (1949). *Ann. Surg.*, **130**, 881.

In describing seven cases of fibrous dysplasia of bone, the authors point out that this condition may easily be confused with single or multiple cysts of bone, with the result that three of their seven patients had been subjected to exploration of the neck for parathyroid tumour, and one of these had died. Fibrous dysplasia is a disease of many synonyms. The condition often begins in childhood with pain or spontaneous fracture. Precocious puberty may occur in females. Irregular areas of rarefaction are seen in radiographs of the bones affected—usually long bones or flat bones. Trabeculation of these areas is common. The histology of the affected bone is characterized by the presence of fibrous tissue and osteoid tissue (young bone as yet uncalcified); vacuolated giant cells with two to ten nuclei were seen in one case. The finding of a normal calcium and phosphorus level in the serum, and of solid tissue on exploration of the bone, are sufficient to exclude hyperparathyroidism, and to spare the patient an unnecessary and possibly dangerous neck exploration. *N. L. Eckhoff.*

**Intravenous Amidopyrine Treatment, with Special Reference to Chronic Articular Rheumatism.** (Beitrag und Kritik zur intravenösen Pyramidonbehandlung unter besonderer Berücksichtigung des chronischen Gelenkrheumatismus.) FÄHNDRICH, W. H., and JUNKERSDORF, J. (1949). *Dtsch. med. Wschr.*, **74**, 845.

A carefully controlled attempt to confirm earlier reports of the beneficial effect in the treatment of rheumatoid arthritis of the intravenous administration of amidopyrine was carried out on 62 cases of acute and chronic forms of the disease, with an equal number of control cases. With either a 10 per cent. or 23·1 per cent. solution, it was found possible to give between 0·5 and 2 g. amidopyrine daily, but only with great care under good clinic conditions. Vomiting, vertigo, and collapse (two cases) were encountered, but no granulocytopenia. There was some improvement in the arthritis as shown by diminution of pain, increased mobility of joints, and lowered erythrocyte sedimentation rate, but the results in treated cases were not significantly better than in the controls. *Dushanka Wolstenholme.*

**Hemangioma of the Knee Joint.** JACOBS, J. E., and LEE, F. W. (1949). *J. Bone Jt Surg.*, **31A**, 831.

The authors present two cases of haemangioma of the knee joint, a rare condition of which approximately thirty cases have been reported in the literature. Less than five of these were diagnosed correctly before arthrotomy. Articular hemangiomata are classified as: (1) juxta-articular—in which, in the knee, there is a palpable tumour involving periarticular structures, particularly the quadriceps muscle; (2) intra-articular—in which the tumour replaces the synovial membrane and anterior fat pad of the knee, with pressure atrophy of articular cartilage and underlying bone as possible sequelae; and (3) a combined type involving both sets of structures. The two cases described belonged to the intra-articular group, and were of a mixed histological pattern—cavernous, capillary, and telangiectatic. Absence of thrombosis is a feature of diagnostic importance. Differential diagnosis has to be made from meniscus lesions, loose bodies, synovitis, haemophilic and haemorrhagic arthritis, and articular tumours. Angiography may be useful in diagnosis. The clinical features in these cases were pain after trauma (which apparently causes haemorrhage), joint effusion, and muscle atrophy. Spontaneous disappearance of the tumour may occur as the result of thrombosis, and this may be aided by *x*-ray therapy, but surgical excision is regarded as the treatment of choice. *W. A. Law.*

**Clinical and Experimental Studies of Salicylic Therapy in Infancy.** (Ricerche clinico-sperimentali sulla terapia salicilica nell'infanzia.) MENGHI, P., and MONTAGNOLO, G. (1949). *Minerva pediat.*, **1**, 423.

**A General Survey of Painful Conditions of the Arm.** (Vue générale sur les algies du membre superieur.) LIÈVRE, J. A. (1950). *Rev. Rhum.*, **17**, 1.

**Some Atypical Clinical Aspects of Early Painful Kyphosis in Adolescents.** (Quelques aspects cliniques atypiques de début de la cyphose douloureuse des adolescents.) CHEVALLIER, M. (1949). *Rhumatologie*, **1**, 273.

**The Surgical Treatment of Certain Forms of Periarthritis of the Shoulder.** (Du traitement chirurgical de certaines formes de peri-arthrite de l'épaule.) DE SÈZE, S., DEBEYRE, J., and DENIS, A. (1950). *Rev. Rhum.*, **17**, 172.

**Periarthritis.** (Periarthrites.) LACAPÈRE, J. (1950). *Rev. Rhum.*, **17**, 59.

**Polyarthritis Precipitated by Myocardial Ischaemia.** KELLY, M. (1950). *Med. J. Aust.*, **1**, 120.

**Rheumatism and the Nervous System. I. The Meningeal Reaction of Rheumatism.** (Rheumatismus und Nervensystem. Die meningealen Reaktionen des Rheumatismus.) SCHEIFFARTH, F. (1950). *Z. Rheumaforsch.*, **9**, 1.

**Epidemic Hepatitis and Rheumatism.** (Hepatitis Epidemica und Rheumatismus.) EPPING, H. (1950). *Klin. Wschr.*, **28**, 92.

**Rheumatic Diseases and the Liver.** (Les rhumatismes et le foie.) BINGEN, E. M., and STOLTE, J. B. (1950). *Rev. Rhum.*, **17**, 53.

**The Sugar Tolerance Curve in Various Rheumatic Conditions.** (Blutzuckerbelastungskurven bei verschiedenen rheumatischen Erkrankungen.) JUNG, A., and BÖNI, A. (1950). *Schweiz. med. Wschr.*, **80**, 185.

**The Significance of Daily Serum-iron and Serum-copper Curves in the Assessment of Rheumatic Conditions.** (Die Bedeutung der Serumeisen- und Serumkupfertageskurven für die Beurteilung rheumatischer Erkrankungen.) BÖNI, A., and JUNG, A. (1950). *Schweiz. med. Wschr.*, **80**, 183.

**Changes in the Blood Chloride Level in Rheumatic Conditions.** (Les modifications de la chloremie dans les affections rhumatismales.) LOUYOT, P., VÉRAIN, M., and VIDAL, —. (1950). *Rev. Rhum.*, **17**, 65.

**"Solucistine" in the Treatment of the Arthroses and Rheumatoid Arthritis.** (La solucistina nelle artrosi e nelle poliartriti croniche.) LANDI, F. (1950). *Policlinico, sez. prat.*, **57**, 133.

**Sodium Gentisate in the Treatment of Rheumatism.** (Il gentisato di sodio nella cura del reumatismo.) TACCONE, G. (1950). *Ann. ital. Pediat.*, **3**, 144.

**The Therapeutic Value in Rheumatic Disorders of Certain Drugs and Dyestuffs with an Inhibitory Action on Hyaluronidase.** (Valore terapeutico nella malattia reumatica di alcuni farmaci e sostanze coloranti ad axione inibitrice sulla jaluronidasi.) PELLEGRINI, P., and MASONI, A. (1950). *Minerva med., Torino*, **41**, 400.

**The Clinical Basis of Treatment of Rheumatic Pain with "Rheumaspray".** (Die klinischen Grundlagen der Behandlung rheumatischer Schmerzen mit Rheumaspray.) KUBELKA, A. (1950). *Wien. med. Wschr.*, **100**, 165.

**The Problem of Rheumatism, with Special Reference to Paul's Cutivaccination.** (Ein Beitrag zum Rheuma-Problem unter besonderer Berücksichtigung der Paulschen Cutivaccination.) LUCKHARDT, A. E. (1950). *Wien. med. Wschr.*, **100**, 183.

**Subacute Articular Rheumatism in the Adult as a Form of Bouillaud's Disease.** (Aux confins de la maladie de Bouillaud. Le rhumatisme articulaire subaigu de l'adulte.) RAVAULT, P., VIGNON, G., and BERTHIER, L. (1950). *J. Méd. Lyon*, **31**, 321.

**Social Aspects of Rheumatoid Arthritis in Denmark.** (La polyarthrite au Danemark dans son aspect social.) NORGAARD, A. (1950). *Sem. Hôp. Paris*, **26**, 1396.

## Sciatica

**Anterior Retromarginal Herniation of the Intervertebral Disk.** (Hernie discale rétro-marginale antérieure.) DE SÉZE, S., and ROTÉS-QUÈROL, J. (1949). *Sem. Hôp. Paris*, **25**, 3964.

The types of herniation of the intervertebral disk which have been described are the common posterior rupture causing sciatica, a second type of herniation through the epiphysial plate resulting in Schmorl's nodes, and, more recently, anterior displacement of the nucleus pulposus, regarded by French authors as a cause of osteophyte formation on the anterior lips of the vertebrae. The authors state, however, that true anterior herniation is rare because of the strength of the ligaments, and describe in this paper the condition which they find more common, in which the herniation forward takes place behind the attachment of the annulus fibrosus, the hernia burrowing obliquely into the spongy bone of the vertebral body. Coincidentally this raises a lip of bone, corresponding to the epiphysial ring. The characteristic lesion is narrow in the antero-posterior direction and broad laterally. A series of tomographs illustrate this very well. Differential diagnosis from Pott's disease is most important, and depends on the facts that the hernia has more definite margins and causes slighter symptoms, while the erythrocyte sedimentation rate is not increased. Less common are confusion with persisting vertebral epiphysis and fracture of the anterior margin of the vertebra.

Mild lumbago may be present, occasionally with some stiffness in the affected segment. There may be also a slight deformity of the vertebral column. There are frequently no clinical signs.

The pathogenesis is discussed. A series of slight injuries, especially before fusion of the epiphysis, may be causative, and non-fusion of the epiphysis is thought to play an important part. The possible relation to Scheuermann's disease is also considered.

*Donald McDonald.*

## Gout

**Treatment of Acute Gouty Arthritis with Pituitary Adrenocorticotropic Hormone (ACTH).** MARGOLIS, H. M., and CAPLAN, P. S. (1950). *J. Amer. med. Ass.*, **142**, 256.

Details of three cases of gouty arthritis treated with pituitary adrenocorticotrophic hormone (ACTH) are given. The first patient was a man of 59 who had had typical recurrent attacks for 16 years. He had been treated during attacks with colchicine and a purine-free diet, and between attacks with a low-purine diet and small doses of colchicine and salicylates. Recurrences continued and became more prolonged on this regime, and the plasma uric-acid content was 5·2 to 5·9 mg. per 100 ml. during the intervals. In a subsequent severe attack the hands, wrists, elbows, shoulders, spine, and feet were all involved and the administration of colchicine, in doses increasing to the point of toxicity, with sodium salicylate and neocincophen, brought only partial relief. The uric-acid level in plasma was now 6 mg. per 100 ml. and the erythrocyte sedimentation rate 29 mm. per hour. The patient was completely disabled and unable to feed himself. A single dose of 50 mg. of ACTH was administered intramuscularly and 75 minutes later he had

practically recovered. He could now feed himself and move hands, elbows, and shoulders without discomfort. Joint tenderness disappeared and he was symptom-free for the first time in 49 days. The plasma uric-acid level was not significantly changed, but he remained free of relapse. [The period of observation since treatment with ACTH is not specified but appears to have been not less than 3 months.]

The second patient, also aged 59, had had six typical attacks in 9 years. In his latest attack symptoms progressed for a month, in spite of treatment with a low-purine diet, colchicine, and sodium salicylate. Maximal doses of colchicine brought no relief; his plasma uric acid-level was 6·5 mg. per 100 ml. and erythrocyte sedimentation rate 15 mm. per hour. He was unable to bear weight on the affected foot. One hour after a single dose of 50 mg. of ACTH he could walk and bear weight with comfort, and he has remained asymptomatic since [approximately 5 months].

The third patient, aged 41, had had recurrent gout for 11 years. An attack of 6 weeks' duration was partially relieved by injection of 50 mg. of ACTH, and a further dose of 25 mg. 6 hours later brought almost complete relief of symptoms, the duration of which could not yet be ascertained.

The authors point out that although administration of ACTH alone will bring relief in an acute attack, a rebound of gouty symptoms will usually occur afterwards. This rebound after the cessation of ACTH therapy may be prevented by giving colchicine or salicylates, or both, immediately after the ACTH. *C. L. Cope.*

## Non-Articular Rheumatism

**Chronic Indurative (Cervical Myalgic) Headache.** STEVENS, R. W. (1950). *Arch. Otolaryng., Chicago*, **51**, 196.

The author believes that the commonest kind of headache found in eye, throat, nose, and ear practice is caused by localized tender thickenings or nodules in the posterior cervical muscles or less frequently in the temporals, masseters, sternomastoids, or the frontal and orbicular muscles. Pain is due to sustained contraction of the muscles. According to the muscles affected the pain may be referred to the temporal or frontal regions or the orbit, less often to the ear, and very rarely to the temporal or masseter muscles, with trismus or pain in the throat on swallowing. After long-continued attacks the pain may become generalized over the whole head. Apart from sinus infections or middle-ear inflammation the condition must be differentiated from the vascular headaches—migraine or histamine headache—or Costen's syndrome.

The headache is usually non-pulsating, which helps to distinguish it from the vascular group. Often, when the pain is worst, the patient is most comfortable sitting up and supporting the head with his hands. Of all headaches [? except those due to intracranial lesions] these are the most sustained. Usually the headache is worse in the morning and gets better during the day as the patient moves about, but if the patient's occupation demands a fixed position of the head (drivers, proof-readers) it increases during the day. As with all headaches it may be made worse by mental strain. Cold draughts are a common cause of increased pain. The majority of cases occur in early and middle adult life, but the condition is found in children, and with increasing age there may be chronic hypertrophic arthritis of the cervical spine.

Wolff and his co-workers have recorded the potentials of the head and neck muscles by electromyography while applying painful stimuli to nose and sinuses. They show that painful stimuli to anterior head structures do not cause referred pain to the back of the head, but that they do cause secondary contracture of the muscles which may persist and be a cause of pain after the stimulus has ceased. They also show that emotional tension is the commonest factor in production of sustained muscular headache. In such subjects minimal stimulation from any cranial structure can intensify already sustained muscular contracture and produce a moderately intense headache. They note too that pain from the soft tissues of the head spreads forward rather than backwards.

Vigorous action potentials can be obtained from the tender nodules but not from non-tender muscles in relaxation. Localized pain and contracture can be produced by injecting 4 to 6 per cent. saline into the neck muscles; injecting procaine hydrochloride into the painful nodules or relaxing them by heat or massage may remove the pain. Histological investigation of the nodules reveals no significant structural change. Probably they are produced by localized spasm, and the pain is due to stimulation of the afferent nerve fibres in the arterial system of the nodule. The peculiar susceptibility of the posterior muscles may be accounted for by the fact that they are postural muscles with a special constant tonus and a lower metabolic rate than other skeletal muscles.

In two years the author saw 100 cases of headache associated with tender cervical muscles; in the same period he saw only ten cases of severe migraine or histamine headache. Of the patients 35 per cent. came for eye examinations and 65 per cent. for nose or ear examination. He emphasizes the comparative rarity of sinusitis as a cause of headache. Proetz puts the incidence at less than 5 per cent. In about 20 per cent. of cases there was a history of some previous head injury. Simons and Wolff believe that, when arachnoid haemorrhage and subdural haematoma have been ruled out, the majority of post-traumatic headaches are due to sustained contracture of the head and neck muscles.

Treatment is by physiotherapy, massage, neck-stretching, and hot and cold showers—three minutes hot to half-a-minute cold—with a small nozzle spray of considerable force. "An unforeseen result of the physical therapy was the discovery of an unsuspected underlying nervous tension and anxiety in a high percentage of the patients. As the physical therapist gained the patients' confidence they gradually revealed many causes of frustration, anxiety, insecurity, or habits not conducive to relaxation and rest."

Procaine hydrochloride was injected into the tender nodules in several cases and gave instant relief, but recurrence was usual and injections are not without danger. They should be used only for acute and early cases where prompt results are desired.

Cases of apparent indurative headache should always be fully investigated for any other condition of the head which might cause a secondary myalgia before physiotherapy is used.

In a discussion before the Chicago Laryngological and

Otological Society (*ibid.*, p. 294) Randolph spoke of food allergy as a cause of myalgia of the posterior cervical muscles. He found that sensations referred to the neck muscles were commonly noticed in allergic patients during the course of individual food tests for the specific diagnosis of food allergy, and that such symptoms could be experimentally produced or relieved by administration or avoidance of specific allergenic foods. A few cases were observed in which similar symptoms could be produced by house dust. His personal experience of antihistaminic drugs was disappointing but, as he remarked, as an allergist he usually saw only the patients on whom antihistamines had been tried already and had failed. *F. W. Watkyn-Thomas.*

**Fibrositis, Tendinitis, Bursitis, and Apophysitis.** (Fibrosites, Tendinites, Bursites, Apophysites.) LACAPÈRE, J. (1950). *Rev. Rhum.*, **17**, 10.

## Endocrinology

**Effect of Deoxycortone and Ascorbic Acid on Formaldehyde-induced Arthritis in Normal and Adrenalectomised Rats.** BROWNLEE, G. (1950). *Lancet*, **1**, 157.

Experiments are recorded to determine whether the beneficial effects of deoxycortone acetate and ascorbic acid in patients with chronic rheumatoid arthritis could be reproduced in formaldehyde-induced arthritis in rats. Three groups of rats were adrenalectomized (full details given) and 1 part in 100 of sodium chloride was added to their drinking water. After 4 days each group was injected in both hind feet with 0·1 ml. of 2 per cent. formaldehyde. The first group was then given 1 mg. deoxycortone subcutaneously daily, the second 20 mg. ascorbic acid intraperitoneally daily and the third 1 mg. of deoxycortone subcutaneously with 20 mg. ascorbic intraperitoneally daily. On the third day all the rats received a second injection of formaldehyde as before. The experiment was repeated on three further groups of normal rats and in both experiments the changes in the inflammatory process that ensued were estimated by measuring, with screw calipers, the linear cross-section at the ankle daily for 10 days. In both the adrenalectomized and normal rats the protection given in the group receiving deoxycortone and ascorbic acid was statistically significantly greater than that afforded by either substance alone. In the adrenalectomized rats the effects in the deoxycortone group and in the ascorbic-acid group were identical, but in the normal rats the protection conferred by ascorbic acid was greater than that given by deoxycortone, which appeared to exacerbate the process. The protection given by 1 mg. deoxycortone with ascorbic acid was similar to that obtained by Selye with 5 mg. cortisone. These results appear to point to the possibility that deoxycortone and ascorbic acid are components of an essential enzyme system in relation to the anti-arthritic steroid hormone. The aggravating effects of unaltered deoxycortone may be due to the competitive substitution of this compound for the naturally-occurring hormone.

These results are thought to substantiate the reports made originally by Lewin and Wassén that simultaneous administration of deoxycortone and ascorbic acid is beneficial in chronic arthritis, and the observation of Selye that prolonged administration of deoxycortone can induce arthritis in rats or may cause exacerbation of formalin-induced arthritis.

[It would have been of interest to know the measurements of a formalin injected lesion over 10 days without any "specific therapy". Perhaps cellulitis would be a better word than arthritis. No body weights are given, and it is not stated whether there was any general water retention in any group.] *Ellis Dresner.*

**Postmenopausal Osteoporosis. Clinical Manifestations, and the Treatment with Oestrogens.** ANDERSON, I. A. (1950). *Quart. J. Med.*, **19**, 67.

Spinal osteoporosis occurring in women at the menopause is regarded as a disease entity rather than as merely one of atrophic processes that characterize advancing age. Considerable speculation exists on the aetiology of the syndrome. The author, believing that the rarefaction of bones is more likely to be due to endocrine imbalance than to dietary deficiency or achlorhydria, studied the effects of a synthetic oestrogen, dienoestrol, on calcium metabolism in women suffering from postmenopausal osteoporosis. He found that dienoestrol promotes calcium retention to its maximal only when the calcium and phosphorus intakes are both about twice the accepted optimal requirement. The suggested treatment for this syndrome, therefore, includes administration of dienoestrol (0·9 mg. daily), vitamin D (up to 10,000 units daily), and calcium glycerophosphate (30 gr. (2 g.) three times a day). Apart from these, protective orthopaedic treatment is recommended in cases with collapse of vertebral bodies.

In post-menopausal osteoporosis serum calcium, serum phosphorus, serum protein, and serum phosphatase levels are normal and the diagnosis therefore rests on the history and the exclusion of the following other conditions causing rarefaction of bones: metastases of malignant neoplasms, osteitis deformans, hyperparathyroidism, multiple myelomatosis, osteomalacia due to steatorrhoea, Cushing's syndrome, and thyrotoxicosis. *S. Karani.*

**Investigations of the Function of the Suprarenal Cortex in Allergic Diseases.** ERIKSSON-LIHR, Z., FORSSELL, P., PETTAY, O., and RUSK, I. (1949). *Acta allerg., Kbh.*, **2**, 299.

The action of the adrenal cortex depends upon its production of three groups of hormones: (1) desoxycorticosterones (salt and water factor); (2) glucocorticosteroids (sugar factor); (3) 17-ketosteroids (protein factor). Various investigations were carried out to see whether in patients suffering from allergic complaints there was a relative insufficiency of the adrenal cortex. It was found that disturbances in carbohydrate metabolism were frequently, and disturbances in water and salt metabolism sometimes, present in allergic cases. No investigations were carried out on the excretion of 17-ketosteroids in such cases. The pituitary adrenocorticotrophic hormone stimulates the production of adrenal cortical hormone at times of stress, and it is suggested by the authors that in allergic diseases the insufficient function of the adrenal cortex does not allow the body to acquire a power of resistance when exposed to physical or chemical stress, so that it enters into a state of exhaustion. This state is seen during the period between attacks when the patient suffers from symptoms of relative lack of cortical hormones. Thus anything that restores or increases the function of the adrenal

cortex will help the organism to overcome the state of exhaustion and prevent the onset of the next state of shock and contra-shock (Selye), which is that of the allergic attack. *A. W. Frankland.*

**The Development of a Refractory State to Adrenocorticotrophic Hormone.** GORDON, G. L. (1949). *Endocrinology*, **45**, 571.

Evidence for the antibody nature of the antihormones produced to heterologous thyrotrophic or gonadotrophic hormones includes the following: (*a*) complement fixation and precipitin formation as an accompaniment of antihormone action; (*b*) times of disappearance and union similar to those of antibody; (*c*) their production by reticulo-endothelial tissue; and (*d*) their localization in the globulin fraction of the serum proteins.

The present study deals with the development of antihormone effects to hog-pituitary adrenocorticotrophic hormone (ACTH) in 28-day Sprague-Dawley rats. Normal rats were divided into three groups. Group I (28 rats) received 1 mg. ACTH intraperitoneally 4 times weekly; Group II (24 rats) received normal saline similarly; Group III (3 rats) received 0·1 mg. ACTH 4 times weekly. Adrenal content of ascorbic acid 24 hours after the last injection was higher in Group I than in Group II at the end of one and two weeks, but fell to values equal to those in controls after 6 weeks. It was, however, not possible to ascribe this to refractoriness, since the constant weekly dose of ACTH became relatively smaller as the rats grew. The response after one hour of rats belonging to Group I to a test dose of ACTH (40 μg. per 100 g.) (assessed by the difference in ascorbic acid content of the left and right adrenal removed before and after the test injection respectively) was greatly decreased (8 to 10 per cent. compared with that in control rats given saline (27 and 25 per cent.) at both 5 and 7 weeks. There was no difference in body weight between the two groups but the adrenal weight was greatly increased in those receiving ACTH at all periods.

Serum from rats of all groups was next injected intraperitoneally into hypophysectomized rats (0·25 ml. on the first and second day and 0·5 ml. on the third day). Four to 6 hours after the last injection the injected rats were tested by receiving 60 μg. ACTH per 100 g., with assay of adrenal ascorbic acid before and after. A marked decrease in the response was noted in the rats injected with serum from Group I compared with that in those given serum from Groups II and III.

No precipitating antibodies were demonstrated *in vitro* when ACTH was used as antigen in concentrations between 0·003 and 0·06 mg. antigen per ml. antiserum. The author suggests that this was because rats in Group I were killed during the negative phase, which is known to follow injection and in the case of antigonadotrophin persists for about 48 hours.

The implications of this refractory state are discussed in the light of administration to man. The dosage is similar and some evidence is available that such a refractory state may develop. There is in addition a possibility that refractoriness to endogenous pituitary hormones may occur.

[For full detail of the techniques used and statistical evaluation the original should be consulted.]

*E. G. L. Bywaters.*

**The Treatment of Chronic Polyarthritis with a Danish ACTH Preparation.** (Behandling af chronisk polyarthritis med dansk ACTH-praeparat.) VERMEHREN, E., and VERMEHREN, M. (1950). *Ugeskr. Laeg.*, **112**, 399.

A 49-year-old man and a 59-year-old woman with rheumatoid arthritis were treated with adrenocorticotrophin obtained from pigs' pituitaries. Characteristic effects were noted on the erythrocyte sedimentation rate, blood picture, and 17-ketosteroid excretion. The condition in the man showed no improvement, and his associated cardiac condition deteriorated considerably (possibly on account of the retention of chloride). The condition in the woman underwent "miraculous improvement", this being associated with a fall in the eosinophil count and a fall in temperature to normal, but relapsed as soon as the treatment was discontinued.

*B. Nordin.*

**Adrenocorticotrophin Treatment of Disseminated Lupus Erythematosus.** (ACTH-Behandling af lupus erythematosus disseminatus.) SCHWARTZ, M., and SONNE, L. M. (1950). *Ugeskr. Laeg.*, **112**, 402.

Two cases of disseminated lupus erythematosus were treated with a Danish preparation of adrenocorticotrophin (ACTH) in doses of 10 mg. two to four times daily for 8 days. In the first case the response was dramatic. Immense subjective and objective improvement occurred within 24 hours. The erythrocyte sedimentation rate (E.S.R.) fell from 130 to 27 mm.; the serum formol-gel reaction became negative; the serum globulin level fell from 4 per cent. to 2·9 per cent.; the excretion of 17-ketosteroids rose by 1,000 per cent., and there was a distinct rise in blood pressure. Deterioration set in immediately treatment was stopped, but 3 weeks later the patient's condition was still better than it had been before ACTH treatment. In the second case no clinical improvement occurred and the patient complained of considerable discomfort. There was, however, a rise in the albumin globulin ratio, and the formol-gel reaction became negative. There was temporary pyrexia after treatment. A third patient was given 4 mg. four times daily for 5 days and the condition responded well. The E.S.R. fell from 80 to 30 mm. and the serum globulin level from 3·8 to 2 per cent. *B. Nordin.*

**Pituitary Implantation in Rheumatoid Arthritis.** (Hypofysinplantation vid kronisk artrit.) EDSTRÖM, G. (1949). *Nord. Med.*, **43**, 263.

Following the introduction of adrenocorticotrophic hormone treatment for rheumatoid arthritis, the author has resumed an experiment on which he originally reported in 1942. In nine cases in which rheumatoid arthritis had been present for not more than four years calf or human foetal pituitary was implanted in September, 1949, and six of these patients have since been discharged without subjective or objective joint symptoms, with a low erythrocyte sedimentation rate (below 10 in all but one), and in good general condition. Increased mobility and reduced oedema were observed in the joints within 24 hours of the implantation, and subsequently the weight rose and the sedimentation rate fell. There was a fall in the eosinophil count and a rise in 17-ketosteroid excretion. The results were better in patients below 40 years than in older patients. *B. Nordin.*

**Anemia and Arthritis in a Case of Pituitary Insufficiency Confirmed at Autopsy.** [In English.] HORTLING, H. (1949). *Acta endocrinol., Kbh.*, **3**, 181.

The case is reported of a man aged 54 years with symptoms of Simmonds's disease which had progressed for 19 years. He died of cachexia and was found to have extensive fibrosis of the pituitary gland. Two years before death he fell and injured his right knee, in which arthritis and ankylosis subsequently developed. The relation of arthritis to Simmonds's disease is discussed.
*A. C. Crooke.*

**Anatomic Changes Produced in Mice Treated with Excessive Doses of Cortisone.** ANTOPOL, W. (1950). *Proc. Soc. exp. Biol., N.Y.*, **73**, 262.

Immature mice received a daily injection of 1·25 mg. of cortisone for 6 days and mature mice were given double this dose for nine days. All the mice lost weight and many of them died. The treatment produced a fall in lymphocyte count and a corresponding increase in the polymorphonuclear leucoctye count. Pathological findings included necrotic foci in the liver, retarded development of the testes or suppression of spermatogenesis, and a failure to withstand infection (granulomatous nodules containing *Corynebacterium pseudotuberculosis murium* were found in the treated mice but not in control mice) or stress (leakage from a water bottle damped one of the cages and all the mice in it died within 48 hours). Weight loss was particularly great in the following tissues and organs: fat, hibernating fat, thymus, spleen, and salivary glands.

The general effects resembled the general adaptation syndrome though the adrenal cortex was atrophied. This suggests that the steroid produces the effects directly and its excess in the circulation suppresses adrenocorticotrophin secretion by the hypophysis. *Peter C. Williams.*

**Adrenocorticotrophic Effect of Stress After Severance of the Hypothalamo-Hypophyseal Pathways.** FORTIER, C., and SELYE, H. (1949). *Amer. J. Physiol.*, **159**, 433.

Male rats were divided into three groups. The first (10) served as normal controls, the second (6) were hypophysectomized, and the third (8) were partially hypophysectomized by removal of the rostral part of the anterior lobe and the whole of the posterior lobe. All the rats had a left adrenalectomy 48 hours after the operation and were then exposed to cold (0° C.) for one hour and killed. The ascorbic acid content of the left and right adrenal glands was compared. A great difference was observed between the content of the two glands in the control group and no difference in four rats of the hypophysectomized group, in which hypophysectomy was proved to have been complete. The third group in which the hypothalamo-hypophysial pathways were severed did not differ significantly from the control group.

In a second experiment the pituitary glands of freshly killed rats were aspirated into a needle and injected into the anterior chamber of the eye of eighteen other rats, which were hypophysectomized 24 hours later. Four weeks later left adrenalectomy was performed, the rats were exposed to cold for one hour, the right adrenals were removed, and the ascorbic acid contents of the two glands was compared. In four of the eighteen rats it was proved that transplants were viable and that hypophysectomy had been complete, and their adrenal ascorbic acid contents were compared with those of normal controls similarly exposed to cold. The reduction in ascorbic acid content of the right adrenal glands of the experimental animals did not differ significantly from that of adrenals in the controls. These experiments are regarded as evidence that the denervated pituitary gland functions and is capable of responding to acute stimulation in the absence of neurological connexions. *A. C. Crooke.*

**Discharge of Adrenocorticotrophic Hormone From Transplanted Pituitary Tissue.** CHENG, C. P., SAYERS, G., GOODMAN, L. S., and SWINYARD, C. A. (1949). *Amer. J. Physiol.*, **159**, 426.

Male rats were hypophysectomized and their pituitary glands were collected in saline. The glands were then grafted either into their original sites in the sella turcica, or into the eye or the spleen; in thirteen of 36 rats so treated histologically viable grafts of glandular cells were subsequently found. These rats together with control groups of normal and of hypophysectomized non-grafted rats received intravenous injections of histamine (1 mg. per 100 g. body weight) after preliminary left adrenalectomy. One hour later the right adrenal was removed and the ascorbic acid content of the two adrenal glands was compared. The ascorbic acid content of the left adrenal glands of the grafted rats was intermediate between that of the normal and the hypophysectomized controls, indicating some functional activity of the graft. An hour after histamine injection the fall in ascorbic acid content, as measured by the difference between left and right adrenal gland contents, was also intermediate between those in normal and hypophysectomized controls. This showed that the grafts were able to respond to acute stimulation in the absence of a neurological or a vascular portal system as described by Harris, although they were too small to allow normal growth or prevent atrophy of the adrenal cortices. *A. C. Crooke.*

**The Effect of Adrenocorticotrophic Hormone (ACTH) and Adrenocorticotrophically Active Peptides (ACTH Peptides) on the Circulating Eosinophils and Urinary Excretion of Adrenaline and Non-adrenaline in a Human Subject.** [In English.] VON EULER, U. S., and LUFT, R. (1949). *Acta endocrinol., Kbh.*, **3**, 323.

Further studies have been made in Stockholm on a 58-year-old patient with rheumatoid arthritis with regard to the effect of pituitary adrenocorticotrophic hormone (ACTH) on the eosinophil count and on urinary excretion of adrenaline and noradrenaline. These substances were extracted and assayed by observing their effect on blood pressure in the cat, and on isolated hen's caecum. During the administration of ACTH or ACTH peptide, the number of circulating eosinophil leucocytes fell to zero; at the same time there was a decrease in the total urinary excretion of catechols, of which adrenaline rather than noradrenaline was the predominating constituent. *G. S. Crockett.*

**Results of Administration of Adrenocorticotrophically Active Peptides (ACTH Peptides) to a Patient Suffering from Rheumatoid Arthritis.** [In English.] LUFT, R., SJÖGREN, B., and HAO LI, C. (1949). *Acta endocrinol., Kbh.*, **3**, 299.

The authors, working at the Serafimerlasarett, Stockholm, and the University of Upsala, describe the

effects of the preparation of pituitary adrenocorticotrophic hormone (ACTH) and a pepsin digest of ACTH protein in a case of rheumatoid arthritis in a man aged 58. The effect of the two substances was identical: there was great clinical improvement, sodium retention, increase in urinary uric acid and 17-ketosteroid output, and a decrease in the number of circulating eosinophils—all temporary effects manifested only while the preparations were being administered. *G. S. Crockett.*

**Effects of Pituitary Adrenocorticotropic Hormone (ACTH) Therapy.** ELKINGTON, J. R., HUNT, A. D., GODFREY, L., MCCRORY, W. W., ROGERSON, A. G., and STOKES, J. (1949). *J. Amer. med. Ass.*, **141**, 1273.

Adrenal cortical extracts and pituitary adrenocorticotrophic hormone (ACTH) have been found to be effective in the treatment of conditions other than rheumatoid arthritis, such as rheumatic fever, lupus erythematosus, and gout. This response would seem to indicate some relationship between these various diseases (as has previously been suggested by Arnold Rich). This paper deals with the treatment with ACTH of two cases of rheumatoid arthritis, two of disseminated lupus erythematosus, one of dermatomyositis, two of rheumatic fever, and one of status asthmaticus. The purpose of the investigation was to study the clinical course, toxic complications, and the degree of stimulation and response of the suprarenal gland. These changes were assessed by means of eosinophil and total leucocyte counts and estimations of the sodium, potassium, chloride, and nitrogen balance, and the output of urinary 17-ketosteroids. Two patients, one with arthritis and one with lupus erythematosus, relapsed completely, despite prolonged treatment and increased dosage, while two others, one with lupus erythematosus and one with dermatomyositis, remained in remission. In one case of arthritis and in the case of asthma the response to the drug was dramatic. In five cases there was an eosinophilic leucopenia following treatment, and in all cases the sodium content of urine was reduced. Consistent changes in the serum sodium and chloride levels were not found. The effects on the serum potassium content and the nitrogen balance were equivocal. It would appear that administration of ACTH decreases carbohydrate tolerance, as thirteen patients developed a slight glycosuria. The excretion of 17-ketosteroids was increased in all cases. Severe potassium deficiency and also encephalopathy, either drug-induced or due to the disease, occurred in the case of acute dermatomyositis. One patient with acute rheumatoid arthritis developed signs of Cushing's syndrome after prolonged treatment; there was, however, neither hypertension nor diabetes. One case failed to respond and the patient died, the presence of antihormones being a possible explanation.

It is concluded that adrenocorticotrophic hormone obviously exerts a profound influence on collagen disease. Presumably it acts by " supporting " the adrenal, which is adversely affected in these hypersensitive states. The technique of repeated short courses of treatment may help to prevent toxic manifestations. The authors sound a wise warning against administration of the drug without laboratory control. *Paul B. Woolley.*

**Effects of Reichstein's Compound S, Pregnenetriolone Acetate, and 17-Alpha Hydroxyprogesterone in Rheumatoid Arthritis.** TERRY, L. L., and LONDON, F. (1950). *Proc. Soc. exp. Biol., N.Y.*, **73**, 251.

**Therapeutic Action of a Vegetable Steroid (S.49-Neocortone) in Acute and Chronic Joint Rheumatism.** (Sull'azione terapeutica di uno steroide vegetale (S.49-neocortone) nelle artropatie reumatiche acute e croniche.) ALLEGRI, A. (1950). *Minerva med., Torino*, **41**, 246.

**Endocrine Imbalance in Rheumatoid Arthritis and Rheumatoid Spondylitis: Hyperglycemia Unresponsiveness, Insulin Resistance, Increased Gluconeogenesis, and Mesenchymal Tissue Degeneration. A Preliminary Report.** LIEFMANN, R. (1950). *Acta med. scand.*, **136**, 226.

**Isolation of 17-Hydroxy 11-Dehydro Corticosterone (Kendall's Compound E) from Urine of Normal Males.** SCHNEIDER, J. J. (1950). *Science*, **111**, 61.

**Studies on Pituitary Adrenocorticotrophin. I. Ultrafiltration of the Hormone.** CORTIS-JONES, B., CROOKE, A. C., HENLY, A. A., MORRIS, P., and MORRIS, C. J. O. R. (1950). *Biochemical J.*, **46**, 173.

**Relation of Pituitary-Adrenal Function to the Rheumatic Diseases.** GRIER, G. S. (1950). *Va. med. Mon.*, 77, 66.

**The Implantation of Stilboestrol in the Treatment of Rheumatic Disorders.** (Les implantations de stilboestrol dans le traitement des rhumatismes.) DAUBRESSE, E. (1950). *Paris méd.*, **40**, 147.

## General Pathology

**Local Injections of a Preparation of Hyaluronidase in the Treatment of Mucinous Infiltration of the Skin.** BLOOM, D., HERRMANN, F. J., and SHARLIT, H. (1949). *J. clin. Invest.*, **12**, 339.

Hyaluronidase was the name given by Meyer and Palmer to an enzyme found in autolysates of a type II pneumococcus which is capable of hydrolysing hyaluronic acid. The hyaluronidase activity was shown to be similar to the activity of the testicular spreading factor of Duran-Reynals, and it is now widely accepted that the two factors are identical.

In two patients with mucinous infiltrations of the skin treated by local injections of hyaluronidase some improvement was noted. The authors make no particular claims, stating that no control injections with other materials were made and that 'the hyaluronidase used may have been inactivated during its preparation for injection. There is a good review of the literature.
*James Marshall.*

**Local Injections of a Preparation of Hyaluronidase in the Treatment of Localized (Pretibial) Myxedema.** GRAIS, M. L. (1949). *J. clin. Invest.*, **12**, 345.

The author reports the case of a 41-year-old woman who, for cosmetic reasons, desired treatment for a plaque of localized myxoedema on each shin. These plaques had been unaffected by thyroid extract and propylthiouracil. The left leg was treated by local injections of hyaluronidase, of which a dose of 300 turbidity-reducing units produced systemic symptoms, but smaller doses gave only local reactions. The size of

the plaque was considerably reduced by the treatment. It is suggested that this was the result of hydrolysis of the hyaluronic acid contained in the skin; but foreign-protein reaction cannot be ruled out, especially as there is some doubt about the amount of active enzyme in the preparation used. The plaque on the right leg, which was treated by incisions to allow mechanical drainage of mucin, also became much smaller. *James Marshall.*

**The Role of Allergy in the Pathogenesis of Rheumatic Fever.** FISCHEL, E. E. (1949). *Amer. J. Med.*, **7**, 772.

**Salicylic Acid Levels in Man.** (Curvas de salicilemia en el hombre.) RUIZ MORENO, A., LITTER, M., and DE LITTER, D. K. (1949). *Bol. Liga argent. Reum.*, **12**, 11.

**Blood Albumin Changes in Chronic Polyarthritis.** (Bluteiweissveranderungen bei chronischer Polyarthritis.) FRITZE, E., and ZEZSCHWITZ, F. v. (1949). *Z. Rheumaforsch.*, **8**, 235.

**Hepatic Function in Primary Chronic Polyarthritis and in Relation to Chrysotherapy.** (La fonction hepatique lors de la polyarthrite primaire chronique et en rapport avec la chrysotherapie.) DE BLÉCOURT, J. J. (1949). *Rev. Rhum.*, **16**, 608.

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# OBITUARIES

## RONALD GREY GORDON

In a happy community of medical men there is usually one leader, or "father" physician, to whom all turn when any difficult decision is necessary. Such was the position of R. G. Gordon, in Bath, ever since this community lost F. G. Thomson during the war.

He died on April 26, of a sudden cerebral haemorrhage, at the age of 61 and, as many of us would wish for ourselves, dropped in his tracks while still in harness. His health had not been good since he was invalided from West Africa with amoebic dysentery in 1944. He had there had command of a General Hospital, from the time when the 4th Southern General Hospital (T.A.), formed by him in 1938 at Bath, was disbanded in 1942.

He was educated at Charterhouse and Edinburgh University; he gained his M.B. in 1911, and M.D. in 1913. In 1926 he became D.Sc. and a Fellow of the Royal College of Physicians, Edinburgh, where he was a Morison Lecturer. He was a man of wide medical interests and, though he wrote with Thomson in 1926 one of the best books on rheumatic diseases of that decade, his main speciality was the nervous system, psychiatry, and child guidance work. On his retirement from the active staff of the Royal United Hospital, he had become part-time geriatrician to the Bath Clinical area, and he was still, at the time of his death, Physician to the Bath and Wessex Orthopaedic Hospital and a Consultant Physician to the Royal National Hospital for Rheumatic Diseases at Bath.

Perhaps R. G. Gordon will, however, be best remembered for his abilities in organizing and his work for the B.M.A. He was for many years a member of the Council, and did a great deal in connection with the change of format of the *British Medical Journal*. As a Chairman of Committee he had the rare knack of knowing when to be patient, when to intervene, and what to say in summing up any difficult discussion.

In 1920 Gordon was first appointed to the staff of the Royal National Hospital for Rheumatic Diseases—then named the Royal Mineral Water Hospital. He was a member of the organizing committee of the Conference on Rheumatic Diseases held at Bath in 1928, and edited the Proceedings of the Conference, to which he contributed a paper on "The Effect of Environment on the Chronic Rheumatic Diseases". He was Chairman of the organizing committee of the International Conference on Rheumatic Diseases held at Bath in 1938, and, in addition to writing his excellent book with F. G. Thomson in 1926, contributed a section on "The Autonomic Nervous System in Rheumatoid Arthritis" to the *Royal National Hospital, Bath, Bicentenary Survey of Chronic Rheumatic Diseases* (1938), and articles on "Gout—an Unsolved Problem" (with J. Barnes Burt, 1939) and "The Nature of Fibrositis and the Influence of Psychological States upon It" (1940) to this Journal. His greatest contribution to rheumatology was, however, his sanity in outlook and, being a physician first and specialist second, the balance of his judgment was always of the greatest value.

As a man he was admired and respected by all, and there could be no more pleasant colleague with whom one might have the privilege of working. He leaves a widow and two sons, both of whom are following in their father's footsteps, one being already a member of the Royal College of Physicians of London. G. D. KERSLEY.

## MATTHEW BURROW RAY

Dr. Matthew B. Ray died at an advanced age on July 5 in a London nursing home. He graduated M.B., C.M., in the University of Edinburgh in 1893 and proceeded M.D. in 1903; in 1934 he took the M.R.C.P. examination. With his death there also passed away yet another of those few remaining ties with the period when a " good physician " earned this title because there was something born and bred in him quite incapable of being acquired. This inner fire never glowed more brightly than in Dr. Ray's last illness, when the gallant courage with which he fought his infection won his doctor's admiration.

So through all his life, quiet, intense, loyal application to the work that was his duty at the time has been the keynote of his character. These traits were seen during the first world war when he won the D.S.O., and was A.D.M.S. of his division with the rank of Colonel. They appeared again when he was quietly hammering with the late Dr. Fortescue Fox at the doors of the British Red Cross Society to give a lead in the treatment of rheumatism and arthritis in London.

The fruit of these endeavours is known and respected throughout the world as the Arthur Stanley Institute for the Rheumatic Diseases, now an integral part of the Middlesex Hospital. Dr. Ray was the senior of the five physicians that constituted the original honorary staff, and after the Institute (then known as the British Red Cross Society Clinic) had become an established entity, he became the first chairman of their honorary medical committee. In recognition of his services in the foundation and development of the Institute, the governing body of the British Red Cross Society passed a special resolution that he should remain a member of the full active staff as long as he so wished. It would have been his wish to have served the Institute to the end, but this was not to be. The coming of the Health Acts brought about the absorption of the Clinic into the nearby Middlesex Hospital, and entailed the cancellation of this recognition. Dr. Ray was therefore transferred to the Consulting Staff, but he continued to attend the Marylebone Dispensary with the same remarkable regularity and loyalty that he had shown throughout the twenty years of his association with the Clinic and Institute.

Dr. Ray's knowledge of hydrotherapy and of spas at home and abroad was most extensive, and when his help in selecting a suitable technique or place of treatment was sought, this knowledge was readily and helpfully given.

Besides his sound clinical ability, and the great devotion apparent in his medical work, Ray had two important hobbies: painting and carpentry. He exhibited regularly in the annual exhibitions of the Medical Art Society and was a skilled cabinet-maker. It is perhaps not insignificant that in his steadfastness and simplicity of character he combined the calling of physician and healer with a practical skill in carpentry, thus following in the steps of the Great Healer as he went about doing good.

C. B. HEALD.